

PUBLIC LIBRARY

JUN 29 1939

DETROIT

SOCIAL SCIENCES

Public Health Reports

VOLUME 54

JUNE 16, 1939

NUMBER 24

IN THIS ISSUE

The Present Poliomyelitis Situation No Cause for Alarm

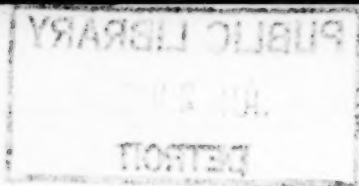
Skin Tests and Serum Antibodies in Pneumonia Immunity

Use of Chick Embryo in Preparing Spotted Fever Vaccine

Preserving Encephalitis Viruses by Freezing and Drying

Summary of Vital Statistics for the United States, 1937





UNITED STATES PUBLIC HEALTH SERVICE

THOMAS PARRAN, *Surgeon General*

DIVISION OF SANITARY REPORTS AND STATISTICS

CHARLES V. AKIN, *Assistant Surgeon General, Chief of Division*



The PUBLIC HEALTH REPORTS, first published in 1878 under authority of an act of Congress of April 29 of that year, is issued weekly by the United States Public Health Service through the Division of Sanitary Reports and Statistics, pursuant to the following authority of law: United States Code, title 42, sections 7, 30, 93; title 44, section 220.

It contains (1) current information regarding the prevalence and geographic distribution of communicable diseases in the United States, insofar as data are obtainable, and of cholera, plague, smallpox, typhus fever, yellow fever, and other important communicable diseases throughout the world; (2) articles relating to the cause, prevention, and control of disease; (3) other pertinent information regarding sanitation and the conservation of the public health.

The PUBLIC HEALTH REPORTS is published primarily for distribution, in accordance with the law, to health officers, members of boards or departments of health, and other persons directly or indirectly engaged in public health work. Articles of special interest are issued as reprints or as supplements, in which forms they are made available for more economical and general distribution.

Requests for and communications regarding the PUBLIC HEALTH REPORTS, reprints, or supplements should be addressed to the Surgeon General, United States Public Health Service, Washington, D. C. Subscribers should remit direct to the Superintendent of Documents, Washington, D. C.

Librarians and others should preserve their copies for binding, as the Public Health Service is unable to supply the general demand for bound copies. Indexes will be supplied upon request.

UNITED STATES GOVERNMENT PRINTING OFFICE, WASHINGTON: 1939

For sale by the Superintendent of Documents, Washington, D. C.

Price 5 cents. Subscription price \$2 a Year

Public Health Reports

Vol. 54 • JUNE 16, 1939 • No. 24

POLIOMYELITIS IN THE UNITED STATES

With the tourist season in full swing, widespread interest in the possible danger from poliomyelitis has been manifested in numerous inquiries to the Public Health Service and to State and local health departments.

A study of the distribution of this disease since January 1939 shows that the incidence of poliomyelitis remained lower than the expectancy, according to the 5-year median, throughout the United States until the recent outbreak in South Carolina. At the present time the condition is apparently on the decline in South Carolina and nowhere else is poliomyelitis sufficiently prevalent to cause alarm.

For the week ended June 10, 1939, there were 54 cases of poliomyelitis reported from the entire country as compared with 60 cases for the preceding week and with 38 cases for corresponding weeks of the 1934-38 period.

VITAL STATISTICS SUMMARY FOR THE UNITED STATES 1937

A summary of the final tabulation of natality and mortality figures for 1937, from the Bureau of the Census, Department of Commerce, was published in the Public Health Reports for January 20, 1939, and provisional figures for 1938 appeared in the Public Health Reports for February 17, 1939. In a recent report¹ the Census Bureau presented a summary of the data for 1937 by race and sex and by States, according to place of residence, and a brief interesting analysis on the basis of other factors. As the tabulation of these data by residence has only recently been begun by the Census Bureau, and as, in some instances, the reassignment of the figures on this basis may affect the rates, the tabulations are presented here as of special value to health officers and other persons interested in vital statistics.

Table 1 summarizes the natality and mortality data for the 11-year period 1927-37, and the accompanying chart shows graphically the trends in the birth and death rates during that period. In 1937 there was a net natural increase of 5.8 per 1,000 population; but, as is well known by students of population, the excess of the crude birth rate over the crude death rate does not give an accurate index to the *future* natural growth of our population. Both the birth rate and the death

¹ Vital Statistics—Special Reports, vol. 6, No. 57, April 29, 1939.

rate are affected by the age distribution of the people, and this is undergoing a change with a shift toward the older age groups. This change, for biological reasons, will tend to produce a continued reduction in the birth rate and it will operate to check any further great reduction in the general death rate.

It is of interest to note the continued decrease in the infant mortality rate, which was 68.7 in 1928, 57.1 in 1936, and 54.4 in 1937.

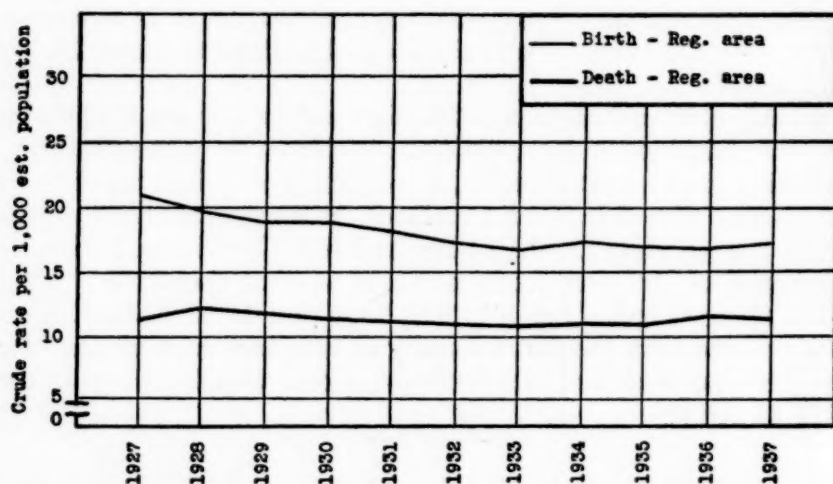


FIGURE 1.—Crude birth and death rate trends in the United States registration areas, 1927-37.

The continued lowering of this rate may tend to retard the approach to a stabilized population and, of course, it contributes to the increasing life expectancy at birth.

TABLE 1.—Summary of vital statistics data for the registration areas of the United States, 1927-37

Year	Percent of total population in registration areas		Number		Crude rate (number per 1,000 estimated population)		Births per 100 deaths	Death rate (number per 1,000 live births)		Death rate (number per 100,000 estimated population)			
	Birth	Death	Births	Deaths	Births	Deaths		Infant mortality	Maternal mortality	Tuberculosis	Cancer	Motor vehicle accidents	
1937	100.0	100.0	2,203,337	1,450,427	17.0	11.2	152	54.4	4.9	53.6	112.0	30.7	
1936	100.0	100.0	2,144,790	1,479,228	16.7	11.5	145	57.1	5.7	55.7	111.0	29.7	
1935	100.0	100.0	2,155,105	1,392,752	16.9	10.9	155	55.7	5.8	55.0	107.9	28.5	
1934	100.0	100.0	2,167,636	1,396,903	17.1	11.0	155	60.1	5.9	56.6	106.2	28.5	
1933	100.0	100.0	2,081,232	1,342,106	16.5	10.7	155	58.1	6.2	59.5	102.2	24.9	
1932	95.2	96.3	2,074,042	1,308,529	17.4	10.9	159	57.6	6.3	62.8	102.0	23.6	
1931	94.7	96.3	2,112,760	1,322,587	18.0	11.1	160	61.6	6.6	68.1	98.9	27.1	
1930	94.7	96.2	2,203,958	1,343,356	18.9	11.3	164	64.6	6.7	71.5	97.3	26.7	
1929	94.7	95.7	2,169,920	1,386,363	18.9	11.9	157	67.6	7.0	76.0	95.9	25.7	
1928	94.3	95.3	2,233,149	1,378,675	19.8	12.1	162	68.7	6.9	79.3	96.1	23.4	
1927	87.6	91.5	2,137,836	1,236,949	20.6	11.4	173	64.6	6.5	80.9	95.7	21.8	

TABLE 2.—Number of births, deaths, and infant deaths (under 1 year of age), by race and sex, United States, 1937

	Total	White		Negro		Other races	
		Male	Female	Male	Female	Male	Female
Births.....	2,203,337	991,356	937,081	132,990	129,472	6,295	6,143
Deaths.....	1,450,427	702,630	552,157	101,166	86,428	5,038	3,008
Infant deaths.....	119,931	55,505	41,559	11,920	9,593	748	606

TABLE 3.—Number of deaths, according to place of residence, in the United States, 1937

Area	Total deaths in area	Deaths—						Total deaths of residents
		Of nonresidents in area			Of residents in other areas			
		Total	From same State	From other States	Total	In same State	In other States	
United States.....	1,450,427	179,874	151,264	28,610	179,874	151,264	28,610	1,450,427
Alabama.....	30,843	2,441	2,099	342	2,426	2,099	327	30,828
Arizona.....	6,919	1,087	593	494	828	593	235	6,690
Arkansas.....	18,364	1,096	785	311	1,584	785	799	18,852
California.....	80,256	16,234	14,434	1,800	15,062	14,434	628	79,084
Colorado.....	13,833	1,698	1,289	409	1,594	1,289	305	13,729
Connecticut.....	17,892	3,058	2,706	352	3,248	2,706	542	18,082
Delaware.....	3,290	390	247	143	360	247	113	3,260
District of Columbia.....	8,727	911	—	911	404	—	404	8,220
Florida.....	20,960	3,132	1,667	1,465	2,115	1,667	448	19,943
Georgia.....	34,446	1,747	1,462	285	2,021	1,462	559	34,720
Idaho.....	4,752	678	481	197	778	481	297	4,952
Illinois.....	87,739	9,728	8,408	1,320	10,373	8,408	1,965	88,384
Indiana.....	40,929	3,164	2,469	695	3,310	2,469	841	41,075
Iowa.....	26,485	3,031	2,402	629	3,012	2,402	610	26,466
Kansas.....	19,204	2,365	1,808	557	2,459	1,808	651	19,298
Kentucky.....	30,899	2,139	1,767	372	2,440	1,767	673	31,200
Louisiana.....	25,010	3,590	3,292	298	3,586	3,292	294	25,006
Maine.....	11,465	1,204	986	218	1,225	986	239	11,486
Maryland.....	22,083	2,487	1,804	683	2,516	1,804	712	22,112
Massachusetts.....	52,248	8,417	7,466	951	8,319	7,466	853	52,150
Michigan.....	53,472	7,462	6,781	681	7,520	6,781	739	53,530
Minnesota.....	26,905	4,263	3,271	992	3,860	3,271	589	26,502
Mississippi.....	23,856	432	311	121	778	311	467	24,202
Missouri.....	44,974	3,854	2,855	999	3,908	2,855	1,053	45,028
Montana.....	6,128	921	774	147	1,002	774	228	6,209
Nebraska.....	13,199	1,488	1,218	270	1,661	1,218	443	13,372
Nevada.....	1,322	311	234	77	330	234	96	1,341
New Hampshire.....	6,528	846	517	329	849	517	332	6,531
New Jersey.....	45,003	9,563	8,544	1,019	10,190	8,544	1,646	45,630
New Mexico.....	6,422	962	484	478	703	484	219	6,163
New York.....	153,772	20,950	18,644	2,306	20,487	18,644	1,843	153,309
North Carolina.....	33,981	3,764	3,149	615	3,557	3,149	408	33,774
North Dakota.....	5,440	1,093	893	200	1,185	893	292	5,532
Ohio.....	80,189	7,709	6,722	987	7,950	6,722	1,228	80,430
Oklahoma.....	21,313	2,076	1,828	248	2,558	1,828	730	21,795
Oregon.....	12,341	1,817	1,384	433	1,649	1,384	265	12,173
Pennsylvania.....	114,949	12,531	11,345	1,186	13,131	11,345	1,786	115,549
Rhode Island.....	8,334	1,511	1,304	207	1,537	1,304	233	8,360
South Carolina.....	20,540	3,270	3,044	226	3,311	3,044	267	20,581
South Dakota.....	5,959	988	796	192	1,056	796	260	6,027
Tennessee.....	30,232	2,565	1,371	1,194	1,780	1,371	409	29,447
Texas.....	65,448	6,564	5,716	848	6,409	5,716	693	65,293
Utah.....	4,989	788	600	188	723	600	123	4,924
Vermont.....	4,981	331	194	137	416	194	222	5,066
Virginia.....	31,119	4,055	3,514	541	4,281	3,514	767	31,345
Washington.....	19,094	2,785	2,393	392	2,891	2,393	498	19,200
West Virginia.....	19,190	2,600	2,140	460	2,596	2,140	456	19,186
Wisconsin.....	31,973	5,532	4,983	549	5,624	4,983	641	32,065
Wyoming.....	2,430	246	90	156	272	90	182	2,456

TABLE 4.—Number of births, according to place of residence, in the United States, 1937

Area	Total births in area	Births—						Total births of resi- dents
		Of nonresidents in area			Of residents in other areas			
		Total	From same State	From other States	Total	In same State	In other States	
United States.....	2,203,337	330,000	305,763	24,237	330,000	305,763	24,237	2,203,337
Alabama.....	61,611	2,622	2,507	115	2,734	2,507	227	61,723
Arizona.....	10,494	911	870	41	1,055	870	185	10,638
Arkansas.....	35,236	2,895	2,582	313	3,088	2,582	506	35,429
California.....	94,230	22,772	22,519	253	22,926	22,519	407	94,384
Colorado.....	19,610	2,939	2,636	303	2,833	2,636	197	19,504
Connecticut.....	22,774	6,575	6,222	353	6,769	6,222	547	22,968
Delaware.....	4,355	816	678	138	815	678	137	4,354
District of Columbia.....	12,343	2,543	-----	2,543	345	-----	345	10,145
Florida.....	20,507	1,180	1,113	67	1,354	1,113	241	20,681
Georgia.....	64,061	6,269	5,828	441	6,027	5,828	199	63,819
Idaho.....	10,369	1,628	1,348	280	1,681	1,348	333	10,422
Illinois.....	115,282	16,358	15,732	626	17,173	15,732	1,441	116,097
Indiana.....	56,087	6,026	5,270	756	5,764	5,270	494	55,825
Iowa.....	42,105	6,979	6,218	761	6,743	6,218	525	41,809
Kansas.....	29,325	4,452	3,784	668	4,361	3,784	577	29,234
Kentucky.....	56,163	3,701	3,335	366	3,811	3,335	476	56,273
Louisiana.....	46,006	5,404	5,168	236	5,385	5,168	217	45,987
Maine.....	15,246	2,106	1,980	126	2,157	1,980	177	15,297
Maryland.....	27,739	3,198	2,642	556	4,414	2,642	1,772	28,955
Massachusetts.....	61,736	16,316	15,492	824	15,970	15,492	478	61,390
Michigan.....	91,539	13,901	13,467	434	13,897	13,467	430	91,535
Minnesota.....	43,036	7,824	7,101	723	7,761	7,101	660	47,973
Mississippi.....	52,095	5,235	4,919	316	5,243	4,919	324	52,103
Missouri.....	66,951	7,174	6,070	1,104	6,740	6,070	670	66,517
Montana.....	10,248	1,955	1,825	130	2,057	1,825	232	10,350
Nebraska.....	22,270	2,680	2,253	427	2,609	2,253	356	22,199
Nevada.....	1,742	387	313	74	443	313	130	1,798
New Hampshire.....	7,633	1,536	1,087	449	1,383	1,087	296	7,480
New Jersey.....	54,607	20,332	19,878	454	21,220	19,878	1,342	55,495
New Mexico.....	13,837	1,138	922	216	1,180	922	258	13,870
New York.....	185,502	36,533	34,945	1,588	35,965	34,945	1,020	184,934
North Carolina.....	79,080	6,647	6,337	310	6,713	6,337	376	79,146
North Dakota.....	12,637	2,866	2,387	479	2,749	2,387	362	12,520
Ohio.....	107,576	13,699	12,670	1,029	13,428	12,670	758	107,305
Oklahoma.....	41,456	4,035	3,688	347	4,174	3,688	486	41,595
Oregon.....	15,457	3,157	2,781	376	3,015	2,781	234	15,315
Pennsylvania.....	161,288	32,802	31,490	1,312	32,647	31,490	1,157	161,133
Rhode Island.....	10,240	2,770	2,452	318	2,730	2,452	278	10,200
South Carolina.....	40,643	3,978	3,802	176	3,998	3,802	196	40,663
South Dakota.....	11,908	2,345	2,009	336	2,453	2,009	444	12,016
Tennessee.....	51,938	4,233	3,398	835	3,851	3,398	453	51,556
Texas.....	116,057	11,020	10,455	565	11,004	10,455	549	116,041
Utah.....	12,603	1,934	1,593	341	1,665	1,593	72	12,424
Vermont.....	6,326	987	825	162	1,164	825	339	6,503
Virginia.....	51,950	5,608	5,104	504	6,463	5,104	1,359	52,805
Washington.....	25,036	5,963	5,616	347	6,005	5,616	389	25,078
West Virginia.....	42,240	3,309	2,823	486	3,556	2,823	733	42,487
Wisconsin.....	53,543	9,846	9,330	516	9,904	9,330	574	53,601
Wyoming.....	4,536	416	299	117	578	299	279	4,692

TABLE 5.—Number of births, deaths, and deaths under 1 year of age in the United States, 1937, by race

Area	Births				Deaths				Infant mortality	
	Total	White	Negro	Other races	Total	White	Negro	Other races	Total deaths under 1 year	Rate per 1,000 live births
United States.....	2,203,337	1,928,437	262,462	12,438	1,450,427	1,254,787	187,594	8,046	119,931	54.4
Alabama.....	61,611	38,208	23,401	2	30,843	16,528	14,311	4	3,844	62.4
Arizona.....	10,494	9,188	190	1,116	6,919	5,693	248	978	1,267	120.7
Arkansas.....	35,236	26,615	8,611	10	18,364	12,722	5,637	5	1,919	54.5
California.....	94,230	89,745	1,565	2,920	80,256	76,645	1,675	1,936	5,070	53.8
Colorado.....	19,610	19,324	181	105	13,833	13,547	222	64	1,441	73.5
Connecticut.....	22,774	22,157	614	3	17,892	17,439	447	6	921	40.4
Delaware.....	4,355	3,657	697	1	3,210	2,686	604	-----	278	63.8
Dist. of Columbia.....	12,443	8,274	4,044	25	8,727	5,456	3,251	20	751	60.8
Florida.....	29,507	20,564	8,927	16	20,900	13,457	7,487	16	1,765	59.8
Georgia.....	64,061	38,194	25,857	10	34,446	18,512	15,928	6	3,952	61.7
Idaho.....	10,369	10,282	1	86	4,772	4,641	12	99	453	43.7
Illinois.....	115,282	109,422	5,785	75	87,739	81,160	6,496	83	4,967	43.1
Indiana.....	56,087	54,264	1,823	-----	40,929	38,764	2,159	6	2,789	49.7
Iowa.....	42,105	41,801	271	33	26,485	26,179	291	15	1,862	44.2
Kansas.....	29,325	28,350	945	50	19,204	18,041	1,141	22	1,302	44.4
Kentucky.....	56,163	53,051	3,111	1	30,899	26,491	4,408	-----	3,321	59.1
Louisiana.....	46,006	26,534	19,384	88	25,010	13,465	11,524	21	3,020	65.6
Maine.....	15,246	15,207	10	29	11,465	11,414	22	29	996	65.3
Maryland.....	27,739	21,761	5,958	20	22,083	17,087	4,981	15	1,705	61.5
Massachusetts.....	61,736	60,782	919	35	52,248	51,287	891	70	2,723	44.1
Michigan.....	91,539	88,191	3,166	182	53,472	50,486	2,841	145	4,386	47.9
Minnesota.....	48,036	47,426	105	505	26,905	26,485	166	254	1,961	40.8
Mississippi.....	52,095	23,248	28,763	84	23,856	10,009	13,805	42	3,066	58.9
Missouri.....	56,951	53,418	3,516	17	44,974	40,323	4,632	19	3,219	56.5
Montana.....	10,248	9,598	14	636	6,128	5,743	32	353	518	50.5
Nebraska.....	22,270	21,979	175	116	13,199	12,891	228	80	937	42.1
Nevada.....	1,742	1,572	4	166	1,322	1,184	7	131	70	40.2
New Hampshire.....	7,633	7,628	3	2	6,528	6,522	5	1	367	48.1
New Jersey.....	54,607	50,346	4,239	22	45,003	41,671	3,307	25	2,154	39.4
New Mexico.....	13,837	13,210	32	595	6,422	5,948	91	383	1,711	123.7
New York.....	185,502	176,652	8,491	359	153,772	145,707	7,682	383	8,369	45.1
North Carolina.....	79,080	53,664	24,592	824	33,981	21,237	12,549	195	5,180	65.5
North Dakota.....	12,637	12,165	1	471	5,440	5,237	2	201	662	52.4
Ohio.....	107,576	102,023	5,523	30	80,189	74,456	5,712	21	5,332	49.6
Oklahoma.....	41,456	37,616	2,197	1,643	21,313	18,234	2,246	833	2,345	56.6
Oregon.....	15,457	15,264	32	161	12,341	12,126	48	167	642	41.5
Pennsylvania.....	161,288	152,631	8,613	44	114,949	107,580	7,330	39	8,109	50.3
Rhode Island.....	10,240	9,954	280	6	8,334	8,129	197	8	487	47.6
South Carolina.....	40,643	19,745	20,860	38	20,540	9,276	11,254	10	3,074	75.6
South Dakota.....	11,908	11,318	6	584	5,959	5,494	10	455	608	51.1
Tennessee.....	51,938	43,859	8,074	5	30,232	22,082	8,148	2	3,171	61.1
Texas.....	116,057	102,129	13,861	67	65,448	53,301	12,117	30	8,575	73.9
Utah.....	12,693	12,547	9	137	4,989	4,876	23	90	526	41.4
Vermont.....	6,326	6,323	3	-----	4,981	4,973	7	1	313	49.5
Virginia.....	51,950	36,834	15,080	36	31,119	19,980	11,117	22	3,619	69.7
Washington.....	25,036	24,370	69	597	19,094	18,502	152	440	998	39.9
West Virginia.....	42,240	39,944	2,292	4	19,190	17,244	1,946	-----	2,610	61.8
Wisconsin.....	53,543	53,007	159	377	31,973	31,561	178	234	2,324	43.4
Wyoming.....	4,530	4,416	9	105	2,430	2,316	27	87	252	55.6

TABLE 6.—*Death rates for selected causes in the United States, 1933-37*

Cause of death ¹	Death rate (number per 100,000 estimated population)				
	1937	1936	1935	1934	1933
Total deaths.....	1,122.1	1,151.8	1,062.2	1,103.2	1,067.1
Typhoid and paratyphoid fever (1, 2).....	2.1	2.5	2.8	3.3	3.6
Measles (7).....	1.2	1.0	3.1	6.5	2.2
Scarlet fever (8).....	1.4	1.9	2.1	2.0	2.0
Whooping cough (9).....	3.9	2.1	3.7	5.9	3.5
Diphtheria (10).....	2.0	2.4	3.1	3.3	3.9
Influenza (11).....	29.4	26.3	22.1	17.3	26.4
Dysentery (13).....	2.3	2.4	1.9	2.7	2.2
Erysipelas (15).....	1.0	1.6	1.7	1.5	1.6
Acute poliomyelitis and acute polioencephalitis (16).....	1.1	.6	.8	.7	.6
Epidemic cerebrospinal meningitis (18).....	1.7	2.4	2.1	1.0	1.2
Tuberculosis of the respiratory system (23).....	49.0	50.6	49.8	51.1	53.6
Tuberculosis (all other forms) (24-32).....	4.6	5.0	5.2	5.5	5.9
Syphilis (34).....	10.2	9.8	9.1	9.3	8.8
Malaria (38).....	2.1	3.1	3.5	3.6	3.7
Cancer of digestive tract and peritoneum (46).....	53.6	53.1	52.1	51.7	50.2
Cancer of uterus and other female genital organs (48, 49).....	15.5	15.4	15.1	14.9	14.4
Cancer of the breast (50).....	10.8	10.7	10.4	10.4	9.9
Cancer (all other forms) (45, 47, 51-53).....	32.1	31.8	30.4	29.1	27.6
Acute rheumatic fever (56).....	1.5	1.7	1.8	1.8	2.0
Chronic rheumatism, osteoarthritis (57).....	1.4	1.4	1.3	1.3	1.3
Diabetes mellitus (59).....	23.7	23.7	22.2	22.1	21.3
Pellagra (62).....	2.5	2.9	2.8	2.8	3.1
Alcoholism (acute or chronic) (75).....	2.6	2.9	2.6	2.9	2.6
Progressive locomotor ataxia (tabes dorsalis), general paralysis of insane (80, 83).....	3.9	4.2	4.3	4.7	4.5
Cerebral hemorrhage, cerebral embolism and thrombosis (82).....	86.5	90.8	85.5	85.4	83.9
Chronic rheumatic heart diseases (90a, 92c, 93e, 95c).....	5.8				
Diseases of coronary arteries and angina pectoris (94).....	54.0				
Heart diseases (all other forms) (90b, 91, 92a, b, 93a-d, 95a, b).....	208.3	265.8	244.9	239.9	227.7
Arteriosclerosis (except coronary), idiopathic anomalies of blood pressure (97, 102).....	17.8	18.6	17.5	18.5	17.3
Pneumonia (all forms) (107-109).....	85.1	93.0	81.9	79.4	69.1
Ulcer of stomach and duodenum (117).....	6.8	6.7	6.6	6.1	6.0
Diarrhea and enteritis (under 2 years) (119).....	11.1	12.2	10.4	13.4	12.5
Diarrhea and enteritis (2 years and over) (120).....	3.5	4.2	3.7	4.9	4.7
Appendicitis (121).....	11.9	12.8	12.7	14.3	14.1
Hernia, intestinal obstruction (122).....	10.1	10.5	10.3	10.3	10.0
Cirrhosis of the liver (124).....	8.5	8.2	7.9	7.7	7.4
Biliary calculi and other diseases of the gall bladder and biliary passages (126, 127).....	6.7	6.9	6.7	7.0	6.9
Nephritis (130-132).....	79.6	83.2	81.2	84.2	82.9
Puerperal septicemia (140, 142a, 145).....	2.9	3.6	4.1	4.0	3.9
Puerperal albuminuria and eclampsia, other toxemias of pregnancy (146, 147).....	2.1	2.2	2.1	2.4	2.4
Other puerperal causes (141, 142b-144, 148-150).....	3.3	3.7	3.6	3.8	3.9
Congenital malformations (157).....	9.2	9.4	9.3	10.0	9.6
Suicide (163-171).....	14.9	14.2	14.3	14.9	15.9
Homicide (172-175).....	7.6	8.0	8.3	9.5	9.6
Automobile accidents (primary) (210).....	28.8	27.8	26.8	26.8	23.3
Other motor vehicle accidents (206, 208, 211).....	1.9	1.8	1.7	1.7	1.6
Other accidents (176-195, 201-205, 207, 209, 212-214).....	50.7	56.0	49.7	51.2	47.4
All other causes.....	145.5	152.6	149.0	153.4	150.4

¹ Figures in parentheses refer to International List titles.

The number of instances of plural births in the United States in 1937 is shown in table 7. The figures include only those cases in which at least one was a live birth. In 1937 there were born in the United States 24,881 sets of twins, 219 sets of triplets, and 4 sets of quadruplets, as compared with 24,569, 277, and 6, respectively, in 1936. The ratios of these figures for multiple births to the total births approximate the ratios based on the frequently mentioned factor of the ascending power of 80, that is the ratio of twins to total births as 1 in 80², of quadruplets, 1 in 80³, and so on. On the basis of this mathematical formula the number of twins in 1937 would have been 27,500, of triplets, 360, and of quadruplets, 4, the last being the actual figure for that year.

TABLE 7.—*Plural births by sex and race in the United States, 1937*

Sex	Cases ¹ of plural births				Sex	Cases ¹ of plural births			
	Total	White	Negro	Other races		Total	White	Negro	Other races
CASES OF TWINS					CASES OF TRIPLETS—continued				
Total.....	24,881	20,972	3,700	119	2 males, 1 female.....	49	44	4	1
2 males.....	8,307	7,094	1,183	30	All living.....	40	36	4	—
Both living.....	7,665	6,622	1,017	26	2 living, 2 M.....	3	3	—	—
1 living.....	642	472	166	4	1 M, 1 F.....	2	1	—	1
2 females.....	8,096	6,849	1,198	49	1 living, F.....	4	4	—	—
Both living.....	7,542	6,425	1,068	49	1 male, 2 females.....	55	43	11	1
1 living.....	554	424	130	—	All living.....	52	42	9	1
1 male, 1 female.....	8,478	7,029	1,409	40	2 living, 1 M, 1 F.....	3	1	2	—
Both living.....	7,897	6,622	1,235	40	CASES OF QUAD-				
1 living.....	240	169	71	—	RUPLETS				
M.....	341	238	103	—	Total.....	4	1	3	—
F.....	—	—	—	—	4 males.....	1	—	1	—
CASES OF TRIPLETS					All living.....	1	—	1	—
Total.....	219	180	37	2	3 males, 1 female.....	1	—	1	—
3 males.....	59	48	11	—	All living.....	1	—	1	—
All living.....	52	43	9	—	2 males, 2 females.....	1	1	—	—
2 living.....	6	5	1	—	All living.....	1	1	—	—
1 living.....	1	—	1	—	1 male, 3 females.....	1	—	1	—
3 females.....	56	45	11	—	2 living, 1 M, 1 F.....	1	—	1	—
All living.....	45	40	5	—					
2 living.....	8	2	6	—					
1 living.....	3	3	—	—					

¹ Includes only those cases in which at least 1 was a live birth.

Births by age of parents are shown in table 8. For 1937 the average age of mothers is stated to be 26.9 years, and of fathers 31.3 years, as compared with 27.0 and 31.5 in 1936.

TABLE 8.—*Births, by age of parents, in the United States, 1937*

Age	Mother	Father	Age	Mother	Father
Total.....	2,203,337	2,203,337	35-39 years.....	201,407	304,415
10-14 years.....	3,142	24	40-44 years.....	65,175	198,890
15-19 years.....	285,173	33,068	45-49 years.....	6,321	77,036
20-24 years.....	692,253	426,617	50-54 years.....	181	27,564
25-29 years.....	583,582	615,519	55 years and over.....	4	16,288
30-34 years.....	362,315	467,497	Not stated.....	3,784	66,449

TABLE 9.—Number of deaths under 1 year, from selected causes, by age, in the United States, 1937

Cause of death	Total deaths under 1 year	Under 1 day	1 day	2 days	3-6 days	1 week	2 weeks	3 weeks	Under 1 month	1-12 months
All causes.....	119,931	32,413	8,214	5,047	8,817	6,484	4,225	3,687	68,887	51,044
Measles (7).....	332	1	—	—	1	2	4	6	14	318
Scarlet fever (8).....	68	—	—	—	—	—	3	—	3	65
Whooping cough (9).....	8,171	1	—	—	5	10	84	104	155	3,016
Diphtheria (10).....	260	1	—	—	4	4	5	9	25	235
Influenza (11).....	3,719	12	8	10	67	119	132	145	493	3,226
Dysentery (13).....	1,074	2	—	2	6	17	12	21	60	1,014
Erysipelas (15).....	270	—	—	—	3	13	28	36	80	190
Encephalitis (lethargic or epidemic) (17).....	22	—	—	—	—	—	—	—	—	22
Meningitis (epidemic cerebrospinal) (18).....	269	—	—	—	—	—	3	1	4	265
Tetanus (22).....	163	2	1	3	45	88	10	3	152	11
Tuberculosis of respiratory system (23).....	287	2	1	1	2	1	3	1	11	276
Tuberculosis of meninges (24).....	209	—	—	1	1	2	1	1	6	203
Other forms of tuberculosis (25-32).....	132	—	—	—	—	2	—	3	5	127
Syphilis (34).....	1,522	234	72	55	99	20	74	85	698	824
Purulent infection, septicemia (36).....	102	—	—	1	6	11	11	5	34	68
Malaria (38).....	226	1	—	5	8	3	4	8	29	197
Other infectious, parasitic diseases (1-6, 12, 14, 16, 19-21, 33, 35, 37, 39-44).....	289	2	1	2	2	8	19	18	52	237
Ricketts (63).....	147	2	1	—	2	3	1	4	13	134
Diseases of the thymus gland (67).....	1,140	125	60	75	93	58	45	57	522	618
Hemorrhagic conditions (70).....	246	12	21	29	62	31	19	16	190	56
Anemias (71).....	169	6	2	9	12	19	10	3	61	108
Encephalitis (nonepidemic) (78).....	104	3	2	—	3	3	2	1	14	90
Meningitis (79).....	557	—	—	—	11	14	13	16	54	503
Cerebral hemorrhage, cerebral embolism and thrombosis (82).....	220	2	3	—	4	4	4	4	21	199
Convulsions (86).....	491	27	18	44	74	46	25	23	257	234
Diseases of ear, mastoid process (89).....	576	1	1	1	1	5	3	10	22	554
Other diseases of nervous system and sense organs (80, 81, 83-85, 87, 88).....	185	10	7	4	16	6	5	4	52	133
Diseases of circulatory system (90-103).....	451	13	5	4	18	33	21	20	114	337
Pneumonia, all forms (107-109).....	16,567	54	135	166	305	701	715	714	2,990	13,577
Other diseases of respiratory system (104-106, 110-114).....	1,226	24	10	15	55	68	55	55	282	944
Diseases of buccal cavity and annexa, pharynx, tonsils (115).....	267	—	—	—	6	17	7	12	42	225
Diseases of stomach (117, 118).....	459	3	5	6	42	33	20	17	126	333
Diarrhea and enteritis (119).....	11,672	14	13	27	122	307	462	438	1,383	10,289
Hernia (122a).....	128	3	1	3	8	2	6	7	30	98
Intestinal obstruction (122b).....	825	2	2	6	34	65	23	30	162	663
Peritonitis (cause not specified) (129).....	134	1	1	—	6	15	10	14	47	87
Other diseases of digestive system (116, 121, 123-128).....	206	1	3	4	15	19	12	5	59	147
Diseases of genitourinary system (130, 131, 133-139).....	462	8	4	14	34	22	23	31	136	326
Diseases of skin, cellular tissue (151-153).....	263	1	1	2	10	50	39	25	128	135
Congenital malformations (157).....	10,169	2,510	791	662	1,331	923	497	424	7,138	3,031
Congenital debility (158).....	3,480	649	226	161	296	231	169	187	1,919	1,561
Premature birth (159).....	33,637	20,272	4,245	1,829	2,621	2,023	957	577	32,524	1,113
Injury at birth (160).....	9,598	5,145	1,419	990	1,355	359	150	78	9,496	102
Other diseases of early infancy (161).....	4,792	1,842	600	519	955	436	183	90	4,625	167
External causes (172-195, 201-214).....	2,381	147	51	40	107	63	63	72	543	1,838
Unknown, ill-defined causes (199, 200).....	6,657	1,259	487	343	741	543	330	287	3,960	2,667
All other causes (45-62, 64-66, 68, 69, 72-77, 154-156).....	607	19	8	11	29	26	13	20	126	418

Table 9 gives the number of deaths under 1 year of age, by cause, and table 10 shows the number of these deaths by certain subdivision age groups of the first year of life and the percent which deaths in the age groups under 6 months are of the total infant mortality. The percentage of infants dying in each of the groups under 6 months was higher in 1937 than in 1927.

The numbers of births and deaths by months and the monthly percent of the total are presented in table 11. While the births show only a slight seasonal variation, with the highest percentages in July, August, and September, the monthly percentages of deaths present the well-known seasonal pattern, with the lowest rates in the summer and early fall and the highest rates in the winter and early spring, when the respiratory infections and their sequellae contribute to the increased toll of lives.

TABLE 10.—*Number of deaths under 1 year of age, by subdivisions of the first year of life, in the registration area, 1927-37*

Year	Number					Percent of total			
	Total deaths under 1 year	Under 1 day	Under 1 week	Under 1 month	Under 6 months	Under 1 day	Under 1 week	Under 1 month	Under 6 months
1937:									
Total.....	119,931	32,413	54,491	68,887	101,881	27.0	45.4	57.4	84.9
White.....	97,064	27,974	46,022	57,309	83,168	28.8	47.4	59.0	85.7
Negro.....	21,513	4,277	8,114	11,075	17,696	19.9	37.7	51.5	82.3
Other.....	1,354	162	355	503	1,015	12.0	26.2	37.1	75.0
1936.....	122,535	32,297	55,210	69,869	103,781	26.4	45.1	57.0	84.7
1935.....	120,138	32,237	54,877	69,834	102,252	26.8	45.7	58.1	85.1
1934.....	130,185	33,300	57,265	73,841	109,528	25.6	44.0	56.7	84.1
1933.....	120,887	31,413	54,744	70,658	102,237	26.0	45.3	58.4	84.6
1932.....	119,431	31,050	54,082	69,496	101,457	26.0	45.3	58.2	85.0
1931.....	130,134	31,786	55,958	73,092	109,005	24.4	43.0	56.2	83.8
1930.....	142,413	33,062	59,922	78,657	118,794	23.2	42.1	55.2	83.4
1929.....	146,661	33,258	60,869	80,063	121,572	22.7	41.5	54.6	82.9
1928.....	153,492	34,234	62,970	83,086	125,898	22.3	41.0	54.1	82.0
1927.....	138,017	32,180	58,724	77,094	115,041	23.3	42.5	55.9	83.4

TABLE 11.—*Number of births and deaths, by month, in the United States, 1937*

	January	February	March	April	May	June	July	August	September	October	November	December
Births:												
Number.....	182,232	170,698	159,650	175,708	181,023	177,588	195,407	201,292	192,513	183,842	172,924	180,460
Percent.....	8.3	7.7	8.0	8.0	8.2	8.1	8.9	9.1	8.7	8.3	7.8	8.2
Deaths:												
Number.....	148,907	137,604	137,512	124,438	119,681	108,155	112,280	103,689	102,730	114,255	112,304	125,272
Percent.....	10.3	9.5	9.5	8.6	8.3	7.5	7.7	7.4	7.1	7.9	7.7	8.7

An interesting table is included in the Census report showing the number of deaths from motor vehicle accidents by the day of the week on which the accident occurred. The number of deaths due to automobile accidents, which constitutes approximately 94 percent of the total in this group, shows the largest toll of lives taken by this cause over the week-end, as would naturally be expected as a result of in-

TABLE 12.—Number of deaths from motor vehicle accidents, by day of accident, in the United States, 1937

Type of accident	Total	Sun-day	Mon-day	Tues-day	Wednes-day	Thurs-day	Friday	Satur-day	Un-known
Total.....	39,643	7,676	4,423	3,819	3,983	4,173	5,064	7,425	3,080
Railroad and automobile (206).....	1,810	274	212	183	191	228	266	312	144
Street car and automobile (208).....	264	73	37	20	28	19	35	36	16
Automobile (210).....	37,205	7,239	4,134	3,579	3,737	3,886	4,719	7,013	2,898
Motorcycle (211).....	364	90	40	37	27	40	44	64	22

TABLE 13.—Number of deaths from cancer, by site and sex, in the registration area

Cause of death	1937		1935		1930 ¹		1925 ¹		1920 ¹	
	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.
Cancers and other malignant tumors (45-53)	67,349	77,425	62,933	74,716	51,777	63,488	41,865	53,639	30,933	41,998
Cancer of the buccal cavity and pharynx (45).....	4,007	974	3,982	923	3,685	869	3,475	759	2,335	462
Lip.....	693	78	671	56	540	46	483	70	393	44
Tongue.....	860	198	878	198	800	147	749	117	609	69
Mouth.....	441	138	441	109	335	104	285	56	176	61
Jaw.....	704	216	776	223	811	240	888	223	856	204
Other and unspecified parts of buccal cavity.....	514	134	466	134	411	109	295	76	211	56
Pharynx.....	795	210	750	203	788	223	775	217	90	28
Cancer of the digestive tract, peritoneum (46).....	37,307	32,028	35,224	31,237	30,431	27,381	25,375	24,080	19,058	19,285
Esophagus.....	2,035	546	1,715	541	1,464	432	1,307	352	871	232
Stomach and duodenum.....	16,150	10,758	16,077	11,027	14,847	10,561	(?)	(?)	(?)	(?)
Intestines (except duodenum, rectum, anus).....	7,175	8,803	6,428	8,037	4,826	6,170	(?)	(?)	(?)	(?)
Rectum and anus.....	4,413	3,481	3,824	3,237	2,764	2,431	2,082	1,959	1,373	1,443
Liver and biliary passages.....	4,418	5,879	4,434	6,045	4,452	5,936	4,028	5,530	3,450	5,193
Pancreas.....	2,594	2,011	2,309	1,809	1,656	1,313	991	911	665	515
Mesentery and peritoneum.....	500	533	424	526	398	497	349	471	259	425
Others under this title.....	22	17	13	15	24	41	25	45	20	34
Cancer of the respiratory system (47).....	5,484	1,872	4,478	1,723	2,688	1,160	(?)	(?)	(?)	(?)
Larynx.....	1,083	154	987	165	854	129	636	138	409	90
Lungs and pleura.....	3,464	1,521	2,951	1,405	1,673	980	989	739	527	429
Other respiratory organs.....	937	197	540	153	161	51	(?)	(?)	(?)	(?)
Cancer of the uterus (48).....	-----	16,338	-----	15,853	-----	14,132	-----	12,377	-----	9,848
Cancer of other female genital organs (49).....	-----	3,643	-----	3,345	-----	2,290	-----	1,674	-----	949
Ovary and Fallopian tube.....	-----	3,018	-----	2,795	-----	1,833	-----	1,218	-----	652
Vagina and vulva.....	-----	577	-----	509	-----	409	-----	398	-----	247
Other female genital organs.....	-----	48	-----	41	-----	48	-----	58	-----	50
Cancer of the breast (50).....	182	13,757	162	13,064	138	10,774	138	8,373	88	6,577
Cancer of the male genitourinary organs (51).....	12,651	-----	11,702	-----	8,661	-----	(?)	-----	(?)	-----
Kidneys and suprarenals (male).....	1,283	-----	1,178	-----	924	-----	717	-----	439	-----
Bladder (male).....	3,084	-----	3,014	-----	2,512	-----	2,095	-----	1,464	-----
Prostate.....	7,490	-----	6,765	-----	4,648	-----	3,668	-----	1,567	-----
Testes.....	466	-----	412	-----	270	-----	227	-----	143	-----
Scrotum.....	24	-----	34	-----	30	-----	16	-----	(?)	-----
Other male genitourinary organs.....	304	-----	299	-----	277	-----	(?)	-----	(?)	-----
Cancer of the skin (52).....	2,048	1,294	2,113	1,278	1,852	1,167	1,636	988	1,505	852
Cancer of other or unspecified organs (53).....	5,670	7,519	5,272	7,293	4,322	5,715	(?)	(?)	(?)	(?)
Kidneys and suprarenals (female).....	-----	879	-----	870	-----	705	-----	541	-----	381
Bladder (female).....	-----	1,567	-----	1,485	-----	1,172	-----	913	-----	650
Brain.....	802	576	654	487	467	337	223	200	96	88
Bones (except of jaw).....	1,017	861	889	875	858	753	591	558	343	406
Other or unspecified organs.....	3,851	3,636	3,729	3,576	2,997	2,748	(?)	(?)	(?)	(?)

¹ The percent of population included in the death registration area for 1920 was 82.3; 1925, 89.6; and 1930, 96.2.² Not comparable.

creased automobile traffic on the highways and probably other factors incident to pleasure seeking. Over 7,000 deaths were recorded as due to automobile accidents on both Saturday and Sunday, as compared with about 4,000 or less for the other days of the week.¹ Friday is the next highest, with nearly 4,719 and Monday next, with 4,134.

Table 13 presents the number of deaths from cancer by principal anatomical site and by sex for 1937 as compared with earlier years. For certain of the earlier years and certain sites the figures are not given, as they are not comparable with those for more recent years, probably because of changes in diagnostic grouping. The cancer death rate was 112.0 per 100,000 population in 1937 as compared with 111.0 in 1936, 107.9 in 1935, and 106.2 in 1934. How much of this increase, as well as that in comparison with rates of still earlier years, may be real or only apparent, because of improved diagnosis, educational work, and greater efforts to discover and treat the disease early, can be determined only by a more detailed analysis of the data. Of course the age distribution and racial composition of the population are important factors in the cancer death rate, and, as has been frequently pointed out, the population is tending to a larger proportion in the older age groups.

STUDIES ON IMMUNIZING SUBSTANCES IN PNEUMOCOCCI

IX. CUTANEOUS TESTS IN NONIMMUNIZED AND IMMUNIZED INDIVIDUALS IN RELATIONSHIP TO SERUM ANTIBODY CONTENT¹

By LLOYD D. FELTON, *Senior Surgeon, United States Public Health Service*, and
PERRY FRANKLIN PRATHER, M. D.

In our study of the evaluation of an antigenic polysaccharide of the pneumococcus from the standpoint of prophylaxis in man, there was found an individual variation in the response to a single injection of a constant dose of antigen (1). This difference in individual

¹ This is one of a series of studies carried out in part under a grant from the Influenza Commission of the Metropolitan Life Insurance Company.

Preceding papers of this series are as follows:

I. Felton, L. D.: Active immunization of white mice by a nonpolysaccharide and probably nonprotein derivative of the pneumococcus. *J. Immunol.*, **23**: 405 (1932).

II. Felton, L. D.: Separation of the organism into acid soluble and acid insoluble fractions. *J. Immunol.*, **27**: 379 (1934).

III. Felton, L. D., Kauffmann, G., and Stahl, H. J.: The precipitation of bacterial polysaccharides with calcium phosphate. *Pneumococcus*. *J. Bact.*, **29**: 149 (1935).

IV. Felton, L. D., Sutliff, W. D., and Steele, B. F.: Antigenic characteristics in man of certain products of the pneumococcus. Comparison with vaccine. *J. Infect. Dis.*, **56**: 101 (1935).

V. Felton, L. D., and Prescott, B.: The effect of alkalis on the immunizing properties of a type I pneumococcus polysaccharide. *Bull. Johns Hopkins Hosp.*, **59**: 114 (1936).

VI. Felton, L. D., and Kauffmann, G.: The essential immunizing antigen of types I and II pneumococci. *Bull. Johns Hopkins Hosp.*, **62**: 430 (1938).

VII. Felton, L. D.: Response in human beings to antigenic pneumococcus polysaccharides types I and II. *Pub. Health Rep.*, **53**: 1855 (1938).

VIII. Ekwurzel, G. M., Simmons, J. S., Dublin, Louis I., and Felton, L. D.: Report on field tests to determine the prophylactic value of a pneumococcus antigen. *Pub. Health Rep.*, **53**: 1877 (1938).

response, as measured by serum antibody content, suggests the possibility of using the antigen as a means of dividing the general population into two groups, the good reactors and the poor reactors, or, perhaps, those susceptible and those not susceptible to pneumococcus infections. Such a possibility rests on two assumptions, both of which are subject to experimental proof: First, that among good reactors the morbidity and mortality rates of pneumonia may be low; and second, that among poor reactors these pneumonia rates may be high. In previous studies, the antigenic response has been determined by the serum antibody content estimated from mouse protection tests. This procedure, since it includes drawing blood, separating the serum, and running protection tests which require the use of a large number of mice, is cumbersome and costly. Therefore, inasmuch as evaluation of any prophylactic measure requires the study of a large sample of the general population, the use of the present mouse method is obviously not satisfactory. For this reason, efforts have been made to test the use of the polysaccharide in a skin test as introduced by Francis and Tillett (2) as a means of measuring response to specific antigenic stimulation. This preliminary report is an attempt to correlate such a skin test with the presence or absence of serum antibodies in groups of individuals before and after immunization.

The observations of Francis and Tillett (2), Finland and Sutliff (3), Finland and Dowling (4), and others, would indicate that the cutaneous test is positive and largely type-specific in human beings when serum antibodies are present. The work by Francis and Tillett was mostly limited to studies on pneumonia patients. The dose of antigen advocated by them was 0.1 cc. of a 1:10,000 dilution, injected intradermally usually in the inner forearms. The test is considered positive when erythema and wheal occur in from 10 to 30 minutes following the injection, when no reaction results from physiological salt solution given at the same time as a control. A delayed test was observed both by Francis and Tillett and by Finland and Dowling, which was largely nonspecific, and perhaps of little significance. These observations have been confirmed by us.

The Francis and Tillett technique was adopted for this study, except that the dose of specific antigen was varied as indicated. The work was begun with a sample of polysaccharide (SSS) prepared by the revised method of Heidelberger, Kendall, and Scherp (5); and for the sake of uniformity this preparation was continued throughout the study. No preservative was used in the skin test antigen. Although it has been found that 0.25 percent phenol apparently does not interfere with the specificity of the reaction, comparative experiments will be necessary before this or any other preservative can be employed. If any is advocated, the control salt solution should contain the same preservative in the same concentration as that in the antigen.

Methods reported elsewhere (1) were used both for immunization and for tests for protective antibody. The dose of immunizing antigen, a mixture of type I and type II active polysaccharides, was in most cases 0.4 mg. of each type, or a total of 0.8 mg. Serum antibodies were estimated by injecting 0.1 cc. serum in a series of mice with variation in culture dilutions of 1:1,000 to 1:100,000,000 in logarithmic series. Blood was drawn before injection of either the immunizing or the skin test antigens. Fourteen or more days after immunization blood was drawn again and a second skin test was done. The first sample of serum was kept in the icebox until the second was obtained. Then the sera before and after immunization were tested on the same day. In reading the skin tests account was taken only of the immediate skin reaction appearing in between 10 and 30 minutes.

In comparing results of cutaneous tests with serum antibody titer, obviously there are four possibilities, namely, positive cutaneous reaction with positive or negative serum antibodies, and negative skin reaction with positive or negative serum antibodies. The relationships of interest here are the "skin-positive-blood-positive" and the "skin-negative-blood-negative" ones. Absolute agreement in these would indicate 100 percent correlation between the results of the two tests. Variation from the absolute may be thought of as percent agreement. The total error comprises the number showing positive skin with negative blood and negative skin with positive blood tests.

The individuals tested in this study were all healthy normal persons from Washington County, Maryland, in and around Hagerstown, and from the Byron Tanneries, Williamsport. With the exceptions subsequently noted, none of the individuals tested had had pneumonia for at least one year prior to this experiment.

EXPERIMENT I. INFLUENCE OF CONCENTRATION OF PNEUMOCOCCUS POLYSACCHARIDE ON INTENSITY OF CUTANEOUS REACTION IN RELATIONSHIP TO SERUM ANTIBODY TITER

Because preliminary tests had indicated that a very small dose of antigen appeared to be more specific than a higher concentration and equally definite in producing the skin reaction, the first experiment was run to ascertain the optimum dose. Sixteen individuals were injected subcutaneously with 2 mg. of type-specific antigens in a 0.5 cc. volume. In table 1 it is seen that, of the 3 individuals immunized with type I, one showed no detectable type I antibodies in 0.1 cc. of the serum, although all 3 had positive skin reactions with the 3 dilutions used.

There were 13 individuals immunized with type II antigen whose sera varied in activity from one in which 0.1 cc. protected mice against 1,000 lethal doses to many which protected against 100,000

lethal doses. It is important to note that the skin tests were all done at one time and that readings, although only roughly quantitative, gave some indication as to the relationship of the intensity of the reaction to the different dilutions of antigen. However, this intensity, indicated by the size of the wheal and the depth of the erythema, showed no relationship to the amount of protective antibody in the serum. For instance, No. 15, an individual whose serum had high protective power, gave a negative skin test with all dilutions of antigen, whereas the 4 individuals who gave the greatest cutaneous response, i. e., No. 8, No. 10, No. 11, and No. 12, had no higher titer of protective antibody than many of the others who gave a less intense reaction.

TABLE 1.—*Influence of concentration of pneumococcus polysaccharide on intensity of cutaneous reaction in relationship to serum antibody titer*

Number	Age	Type of pneumococcus antigen	Cutaneous reaction after immunization			Serum antibodies	
			SSS dilutions			Number of lethal doses against which mice are protected by 0.1 cc. serum	
			1:10,000	1:100,000	1:1,000,000	Type I	Type II
1	49	I	++	+	+	0	10
2	45	I	++	++	+	100,000	10
3	31	I	++	++	+	100,000	100
4	58	II	+	+	0	0	1,000
5	50	II	+++	++	+	0	100,000
6	46	II	++	++	+	0	100,000
7	45	II	++	++	++	0	100,000
8	32	II	++++	+++	+++	100	10,000
9	39	II	+++	++	+	0	100,000
10	50	II	+++	+++	+++	0	10,000
11	45	II	+++	+++	+++	0	10,000
12	45	II	+++	+++	+++	0	100,000
13	32	II	+	0	0	0	100,000
14	43	II	++	+	+	0	100,000
15	31	II	0	0	0	0	100,000
16	40	II	++	++	+	0	100,000

Thus, as shown above in the table, there is no correlation between intensity of reaction to different dilutions and quantity of antibodies. The degree of intensity doubtless depends upon individual characteristics (not related to serum antibodies as measured by the mouse test), such as thickness, texture, and pigment of the skin, and perhaps age of the individual. Furthermore, it would appear that, although the numbers of individuals tested are small, for skin reactions the 1:10,000 dilution of the types I and II polysaccharides as prepared by the recent Heidelberger method is apparently superior to a lower concentration. Consequently, except as noted, this dose has been used throughout.

EXPERIMENT II. CUTANEOUS REACTIONS IN NON-IMMUNIZED CHILDREN
UNDER FIVE YEARS OF AGE

The work of Sutliff (6), Davies (7), Felton (1), Alston and Lowdon (8), and others, indicates that infants failed to respond either to the immunizing antigens or to pneumococcus vaccine, at least to a degree measurable by the presence of protective antibody in the serum. In this experiment, a group of normal children under 2 years of age and from 3 to 5 years was tested to determine the percentage giving a positive skin reaction. Tests were run with 3 dilutions of antigen as in the preceding experiment. Of the group of 17 under 2 years, one child responded against both type I and type II antigens in dilution of 1:10,000 only (table 2). This child, aged 7 months, had been in the hospital 3 months prior to the test with bronchopneumonia, the type of which was not determined. Of the 52 in the group from 3 to 5 years, again only one child gave a positive test with each type, one with type I, another with type II antigen, in dilution of 1:10,000. In the total of 69 children, only these 3 gave positive tests. Since one child gave positive tests against both types, the percentage was 2.9 percent for each type. These results are a confirmation of our observation in which a group of 14 children from 3 to 15 years showed no serum antibodies prior to immunization with active polysaccharide, although all children above 2 years injected with an immunizing dose responded well to the polysaccharide antigen.

TABLE 2.—*Cutaneous reactions in nonimmunized children under 5 years of age*

Age (years)	Number tested	Positive reactions with various dilutions of antigen											
		Type I						Type II					
		1:10,000		1:100,000		1:1,000,000		1:10,000		1:100,000		1:1,000,000	
		Num- ber	Per- cent	Num- ber	Per- cent	Num- ber	Per- cent	Num- ber	Per- cent	Num- ber	Per- cent	Num- ber	Per- cent
Under 2.....	17	¹ 1	5.9	0	0	0	0	¹ 1	5.9	0	0	0	0
3 to 5.....	52	² 1	1.9	0	0	0	0	³ 1	1.9	0	0	0	0
Total.....	69	2	2.9	0	0	0	0	2	2.9	0	0	0	0

¹ One child reacted to both antigens.

² Reacted only to type I antigen.

³ Reacted only to type II antigen.

Our results on infants are in complete contrast to those of Sutliff and Finland (6), who state, "In infants less than 15 months of age, an erythema was invariably produced which obscured any immediate specific erythematous reaction. No wheal formation was observed." Alston and Lowdon (8), in testing 15 infants up to 1½ years of age, failed to observe any reactivity in this age group. The difference in results obtained by Sutliff and Finland, and by Alston and Lowdon

and the present writers can undoubtedly be explained on the basis of the use of different preparations of the polysaccharide. Sutliff and Finland used a sample prepared by the original method of Heidelberger and Avery (9), which, although antigenic for human beings, had low antigenicity for mice; while in both Alston and Lowdon's work and in our own, the preparation used was made by the revised method of Heidelberger and coworkers, a sample very similar to the one used by us previously which was antigenic for both mice and men (1). The difference certainly was due to variation in the antigen and not to the different infants tested. It is pertinent that the preparation used throughout this experiment gave a satisfactory erythematous wheal reaction in adults.

EXPERIMENT III. RELATIONSHIP BETWEEN INTENSITY OF CUTANEOUS REACTIONS AND SERUM ANTIBODY CONTENT

As the work progressed, it became apparent that the degree of correlation was not high between antibody content of the serum and presence of skin reactions of individuals immunized with polysaccharide. In Tables 3A and 3B are given the results obtained in a group of individuals selected from 179 persons, all of whom were immunized at one time with the same dose of a polyvalent antigen and likewise tested for skin reactions. Antibody titer was estimated in serum drawn before and 14 days after injection of the antigen. Twenty men were chosen at random from those who gave positive

TABLE 3A.—*Relationship between intensity of positive cutaneous reactions and serum antibody content*

Name	Age	Cutaneous reaction with SSS dilution 1:100,000		Serum antibodies	
				Number of lethal doses against which mice are protected by 0.1 cc. serum	
		Type I	Type II	Type I	Type II
C. A. S.	61	+	+	5	50,000
J. H.	54	++	++	5	50,000
H. B.	47	+	+	50	50,000
C. W. H.	64	++	++	500	50
P. F. C.	23	+	+	500	500,000
R. P. T.	60	+++	+++	500	500
S. B.	56	+++	+++	500	2,000,000
J. E. Y.	58	+	+	5,000	500,000
C. H.	50	++	++	50,000	50,000
A. K.	46	++	+	50,000	2,000,000
L. M.	30	+++	+	50,000	500,000
L. S.	43	+++	+	50,000	500,000
G. F. R.	32	++	++	50,000	2,000,000
I. C. S.	60	++	++	500,000	500
G. S. L.	32	++	++	500,000	5,000
G. P.	32	+	+	500,000	2,000,000
McK. S.	41	++	+++	500,000	50,000
G. Z.	43	+++	++	500,000	50,000
R. H.	65	+++	+++	500,000	50,000
B. F. T.	55	+++	+++	2,000,000	500,000

skin reactions as well as serum antibodies (table 3A). The intensity of the skin reactions varied, as did also the serum antibody titer. However, as shown in the first experiment, with this group intensity of skin reaction did not correlate with titer of serum antibody. A study of the table will be convincing; for example, G. P. gave a positive (+) skin test against both types I and II, and 0.1 cc. serum protected mice against 500,000 lethal doses of type I and 2,000,000 lethal doses of type II. On the other hand, R. P. T. gave a very definite cutaneous reaction (type I, +++; type II, ++) and yet 0.1 cc. serum protected against only 500 lethal doses of either type I or type II pneumococci.

TABLE 3B.—*Relationship between intensity of negative cutaneous reactions and serum antibody content*

Name	Age	Cutaneous reaction with SSS dilution 1:100,000		Serum antibodies	
				Number of lethal doses against which mice are protected by 0.1 cc. serum	
		Type I	Type II	Type I	Type II
S. B.	30	+	0	0	50
H. G.	44	0	+	0	500
C. R.	51	0	0	50	500
H. R.	44	0	0	50	5,000
F. M.	46	0	0	50	50,000
R. C.	56	+	0	500	5,000
F. M.	24	0	0	500	500,000
N. M.	43	0	++	500	500
A. G.	44	0	0	500	50,000
M. R.	49	++	0	500	0
F. B.	60	+	0	500	500
J. S.	58	++	0	500	500
C. M.	33	++	0	500	5,000
R. D.	48	+	0	5,000	500
W. J.	34	++	0	5,000	5,000
H. C.	32	++	0	5,000	50
R. S.	45	0	0	50,000	50
A. H.	59	++	0	50,000	500,000
S. M.	27	0	0	500,000	500
C. G.	48	0	0	2,000,000	2,000,000

Table 3B shows the 20 individuals among the 179 who failed to give a skin reaction to either one or both types. Thus the lack of correlation between skin test and serum antibody titer is shown more clearly in this group. Negative skin tests were found with individuals whose sera contained protective antibodies against as high as 2,000,000 lethal doses of pneumococci of both types. Yet one individual, S. B., gave a positive skin test against type I antigen when his serum failed to protect against one lethal dose of type I organisms. However, it is possible that if a larger dose of serum had been used in the mouse test, some protection would have been found. In the group of 20, this is the only exception; in all the others a positive test indicates some serum antibody. On the other hand, negative skin tests do not prove

that serum antibody is absent. This list includes all the negative ones among the group of 179 tested at one time; in other words, 11 percent of the group gave negative cutaneous tests, and yet all had antibody in their sera in varying amounts.

EXPERIMENT IV. CUTANEOUS REACTIONS WITH POLYSACCHARIDE ANTIGEN IN THE GENERAL POPULATION, NONIMMUNIZED AND IMMUNIZED

Tables 4A and 4B show the findings on the immunized individuals in whom skin tests were performed. Analysis has been made in age groups (decades), although with the realization that insufficient numbers of each group are included to make advisable deductions as to the influence of age. However, certain conclusions may be drawn. It is true that of the 70 children under 9 years of age, only 4.3 percent gave positive tests with type I antigen, whereas in persons between 20 and 59 years of age, over 50 percent were positive. In the entire group of 137 non-immunized persons, 25 percent gave a positive skin test; deducting the children under 10, the percentage of positive tests is 48. These figures are lower than those of Rogers and Wagner (10) and Alston and Lowdon (8). Whether or not this is the true picture in the nonimmunized population, or whether it varies with geographic location awaits tests on a larger group. Such a study is now in progress.

The numbers of individuals tested after immunization, not necessarily the same individuals, are small, with perhaps the exception of the decade 10 to 19. However, our results would indicate that age does not influence the skin test, at least up to 69 years. The percentage of positive reactions in this entire group of 179 is 84.4 percent, as compared with 48 percent (exclusive of the group under 9 years) among the nonimmunized.

The findings with type II, shown in table 4B, are similar with the exception that before immunization the positive reactions occur in a much smaller percentage of the population, i. e., 7.5 percent of the total of 133, or 11.1 percent exclusive of the age group under 9 years. This percentage is markedly lower than that reported by Alston and Lowdon, who found 63 percent positive to type II in a nonimmunized group. However, after immunization, of the 144 individuals tested by us, 112 or 77.8 percent gave positive cutaneous reactions.

Thus with type I the percentage of nonimmunized persons over 10 years of age giving a positive skin reaction was 48 as compared to 84 percent in the immunized group. With type II, the percentages are, respectively, 11 and 78. In other words, after injection of a polyvalent antigen, skin tests were negative to type I in 16 percent and to type II in 22 percent of the persons tested.

TABLE 4A.—*Cutaneous reactions with polysaccharide antigen in the general population, nonimmunized and immunized*

TYPE I

Age	Nonimmunized			Immunized		
	Number tested	Positive test		Number tested	Positive test	
		Number	Percent		Number	Percent
Under 9.....	70	3	4.3
10 to 19.....	3	1	33.3	64	55	85.9
20 to 29.....	17	10	58.8	24	22	91.7
30 to 39.....	12	6	50.0	26	24	92.3
40 to 49.....	12	6	50.0	33	54	72.7
50 to 59.....	9	6	66.6	15	13	86.7
60 to 69.....	12	3	25.0	10	10	100
70 to 79.....	2	0	0	6	3	50
80 to 89.....	1	0	0
Total.....	137	35	25.5	179	151	84.4

EXCLUDING GROUP UNDER 9 YEARS

10 to 89.....	67	32	47.8
---------------	----	----	------	-------	-------	-------

TABLE 4B.—*Cutaneous reactions with polysaccharide antigen in the general population, nonimmunized and immunized*

TYPE II

Age	Nonimmunized			Immunized		
	Number tested	Positive test		Number tested	Positive test	
		Number	Percent		Number	Percent
Under 9.....	70	3	4.1
10 to 19.....	3	1	33.3	28	24	85.7
20 to 29.....	14	0	0	23	21	91.3
30 to 39.....	11	1	9.1	26	19	73.1
40 to 49.....	12	2	16.6	34	24	70.6
50 to 59.....	9	2	22.2	18	14	77.8
60 to 69.....	12	1	8.3	9	8	88.9
70 to 79.....	2	0	0	5	2	40
80 to 89.....	1	0	0
Total.....	133	10	7.5	144	112	77.8

EXCLUDING GROUP UNDER 9 YEARS

10 to 89.....	63	7	11.1
---------------	----	---	------	-------	-------	-------

In addition, another group of nonimmunized individuals was tested with type III antigen, with the usual 1:10,000 dose. The ages varied from 6 to 65 years, with 50 percent in the 10 to 20 decade. No attempt was made to immunize this group with type III polysaccharide after the skin test. Of the 60 individuals tested, only one gave a positive reaction. This individual, 54 years of age, had type III pneumonia the previous year. The skin tests made with types I and II antigen in this case were also positive, definitely with type I, but only slightly with type II.

EXPERIMENT V. PERCENTAGE AGREEMENT BETWEEN SERUM ANTIBODIES AND CUTANEOUS REACTIONS WITH POLYSACCHARIDE ANTIGEN

The question of correlation of skin tests with antibody is an important one. Groups of persons (tables 5A and 5B) were chosen representing all those on whom both skin tests using polysaccharide antigen, and antibody titrations, were made. In table 5A, the results on 48 nonimmunized individuals show 58 percent agreement between skin tests and type I antibody titer. This figure includes both skin-positive-blood-positive and skin-negative-blood-negative; for type I there were, respectively, 6 and 22 individuals out of 48 in each of these categories. However, when the percentage of skin-positive and blood-positive only is calculated, there is an agreement of only 12 percent for type I in contrast to 46 percent when both skin and blood tests are negative. In other words, 46 percent of the group comprised individuals of different ages giving a negative skin test with negative antibody, and only 12 percent gave positive tests for both. The errors in correlation in the experiment are noted in the column showing lack of agreement in which 12 individuals, or 25 percent, gave a positive skin test when protective antibodies were absent, and 8, or 16 percent, gave a negative skin test when antibodies were present.

TABLE 5A.—Percentage agreement between serum antibodies and cutaneous reactions with polysaccharide antigen

TYPE I

Age	Nonimmunized								Immunized							
	Number tested	S+ B+	S- B-	S+ B-	S- B+	Percent agreement			Number tested	S+ B+	S- B-	S+ B-	S- B+	Percent agreement		
						S+ B+	S- B-	Total						S+ B+	S- B-	Total
10 to 19	0								59	44	3	5	7	74.6	5.1	79.7
20 to 29	10	1	3	3	3	10	30	40	17	12		3	2	70.6		70.6
30 to 39	8	1	5	3	2	12.5	62.5	75	21	19		2		90.5		90.5
40 to 49	9		3	3	3		33.3	33.3	26	15	2	2	7	57.7	7.7	65.4
50 to 59	8	3	2	2	1	37.5	25	62.5	12	11			1	91.7		91.7
60 to 69	11	1	7	2	1	9.1	63.6	72.7	7	7				100		100
70 to 79	2		2				100	100	1	1				100		100
Total	48	6	22	12	8	12.5	45.8	58.3	143	109	5	12	17	76.2	3.5	79.8

S+ = positive skin reaction; S- = negative skin reaction.

B+ = antibodies present in blood; B- = antibodies absent in blood.

After immunization, the correlation between these two tests is better; for among 143 individuals the total percentage agreement was 80 percent, of which 109, or 76 percent, were positive in both tests, in other words, almost a reciprocal relationship to the percentage agreement before immunization. The errors are somewhat smaller in the immunized, since only 8.2 percent of skin-positive were without demonstrable antibodies, and only 11.8 percent were skin-negative when antibodies were present.

TABLE 5B.—Percentage agreement between serum antibodies and cutaneous reactions with polysaccharide antigen

TYPE II

Age	Nonimmunized								Immunized							
	Number tested	S+ B+	S- B-	S+ B-	S- B+	Percent agreement			Number tested	S+ B+	S- B-	S+ B-	S- B+	Percent agreement		
						S+ B+	S- B-	Total						S+ B+	S- B-	Total
10 to 19	0				4				27	23	1		3	85.2	3.7	88.9
20 to 29	10		6		4				16	12	1	1	2	75	6.2	81.2
30 to 39	7		6		1	5	55.7	85.7	21	17			4	80.9		80.9
40 to 49	10		4	1	5		40	40	30	20	2		8	66.7	6.7	73.4
50 to 59	8	1	3	1	3	12.5	37.5	50	14	10			4	71.4		71.4
60 to 69	11		7	1	3		63.6	63.6	7	6			1	85.7		85.7
70 to 79	2		2				100	100	0							
Total	48	1	28	3	16	2.1	58.3	60.4	115	88	4	1	22	76.5	3.5	80.0

S+ = positive skin reaction; S- = negative skin reaction.

B+ = antibodies present in blood; B- = antibodies absent in blood.

As shown in table 5B, for type II the figures are somewhat different. Before immunization, in the group having both tests positive the percentage agreement is as low as 2.1 percent; however, if to this is added the skin-negative-blood-negative, the total percentage agreement is 60.4 percent. On the other hand, after immunization the total percentage agreement is 80.0 percent, of which 76.5 percent had both tests positive. As in type I, the total error after immunization is about 20 percent.

EXPERIMENT VI. PERCENTAGE AGREEMENT BETWEEN SERUM ANTIBODIES AND CUTANEOUS REACTIONS OBTAINED WITH ANTIGEN-ANTIBODY COMPLEX

In the foregoing experiment, the results would indicate that agreement between skin test and antibody content was not ideal. Some years ago, a study was made using SSS-antibody complex as an immunizing antigen in rabbits and in mice.² The complex was also used in a cutaneous test in these animals to detect the presence of serum antibody. It was found that this neutral complex of antigen and antibody gave negative skin tests in highly immunized rabbits, but in normal rabbits a slight but definite positive reaction occurred. This observation to our knowledge has not been made on human beings. It seemed possible that such a test might give better correlation with demonstrable serum antibodies than the one using only the free or uncombined SSS antigen. Hence a preliminary trial was made. The neutral antibody-polysaccharide complex was prepared as follows: The antibody in rabbit serum of high titer was precipitated with such a concentration of SSS that not all antibody present was

² Unpublished data.

entirely thrown down; that is, a slight excess of antibody remained in the supernatant serum. This complex was washed once with physiological saline at 4° C. and then once with water, and was finally diluted with water at room temperature to make a concentration of 1:100,000 SSS, assuming that all the polysaccharide used was precipitated with the antibody. Most of the complex dissolved. It was then filtered, without adding preservative, tested for sterility, and was then ready for cutaneous tests. It is important to note that antigen so prepared, due to dissociation of SSS and antibody, gave a slight precipitate with potent rabbit serum. Both type I and type II antigens were prepared in this manner.

As judged from our experience with rabbits, a positive skin test with this antigen denoted the absence of serum antibodies, whereas a negative skin test gave presumptive evidence that antibodies were present. In other words, the skin reaction would be very similar to that of the Schick test in which a negative reaction means the presence of antitoxin.

A summary of the results obtained in this preliminary study is given in table 6. In the case of type I, of 108 nonimmunized individuals, there was only one who gave both positive cutaneous reaction and positive serum antibodies; 74 were negative in both tests; and 27 had negative skin reactions and positive blood tests. In other words, only 27 out of 108 (25 percent) individuals with positive antibody failed to give a skin reaction. Thus, in this nonimmunized group only 25 percent gave the desired reaction, a negative skin test with serum antibodies present. On the other hand, after immunization of these same individuals, with a few additional persons, 111 out of 117, or 95 percent, gave negative skin tests with positive serum antibodies, while 2 with positive blood tests failed to give negative skin tests.

TABLE 6.—*Percentage agreement between serum antibodies and cutaneous reactions obtained with antigen-antibody complex*

Type	Age	Nonimmunized						Immunized					
		Number tested	S+ B+	S- B-	S+ B-	S- B+	Percent agreement ¹	Number tested	S+ B+	S- B-	S+ B-	S- B+	Percent agreement ¹
I.....	18 to 72	108	1	74	7	27	25	117	2	4	0	111	94.9
II.....	18 to 72	110	1	71	6	32	29	117	9	0	0	108	92.3

¹In this table only, percent agreement indicates skin negative (S-), blood positive (B+). S+=positive skin reaction; S-= skin reaction negative; B+=antibodies present in blood; B-=antibodies absent in blood.

With type II, in the nonimmunized group, 32 out of 110 gave negative skin and positive blood serum reactions, and only 1 failed, giving a positive test in both. The correlation between the two tests was,

therefore, 29 percent. On the other hand, after immunization, 108 out of the 117 gave negative skin tests when serum antibodies were present, and 9 were positive to both these tests. It is pertinent to emphasize that this high degree of correlation between skin test response to complex and serum antibodies occurs only after immunization with the polysaccharide. The lack of agreement in individuals before immunization, that is, those giving both negative skin and negative antibody tests, is greater than when the free SSS antigen is used in the skin test. It would appear that the use of the SSS-antibody complex as antigen in the cutaneous test is significantly superior as an indicator to judge the presence of serum antibody, but only in those immunized by injection of pneumococcus polysaccharide.

These tests were carried out with one preparation of complex antigen in which the concentration based on polysaccharide content was 1:100,000. This concentration was used because from preliminary tests negative reactions occurred in the presence of serum antibodies. If higher concentrations are employed this antigen gives, for the most part, the same skin test as the free SSS antigen of Francis and Tillett. Of necessity therefore an appropriate concentration must be chosen to obtain the desired reaction, a negative skin test in the presence of serum antibody and a positive one in its absence.

DISCUSSION

In this study our interest is primarily limited to the ability of the individual to respond to an immunizing agent as measured by the skin test, with the possibility in mind of determining individual susceptibility to pneumococcus infection. Some individuals shown to be good reactors to the immunizing agent may be separated from others found to be poor reactors. The former are able to develop a high resistance to pneumococcus infection, and if contracting the disease may have a mild attack with recovery assured; whereas the latter are probably the highly susceptible in whom lobar pneumonia may be a very serious infection.

Evidence bearing upon this assumption may be deduced by the results of the skin reaction in cases of lobar pneumonia. For instance, in the original description of the cutaneous test by Francis and Tillett, it is reported that recovery from type I pneumonia in serum-treated cases was invariably accompanied by the development of positive skin reaction to type I SSS. In contrast, only 50 percent of the non-serum-treated type II and III cases who recovered gave a specific response to the homologous SSS. These authors also stated that "antibodies might be present in the blood of the patient, and the skin test remain negative. When, however, the skin test became positive, recovery invariably ensued." In a later publication, Francis (11) showed that all but one of 46 convalescent cases treated with

type I pneumococcus serum gave a positive cutaneous reaction. In 7 fatal cases, the skin reactions were persistently negative, even in the presence of circulating type-specific antibodies. Finland and Sutliff (3) in a series of 41 cases not serum-treated reported that 30 recovered, of whom 17 gave a positive homologous skin test. Of 11 fatal cases only one showed a positive homologous reaction. In this patient positive tests were elicited 36 and 12 hours before death, and in both instances cultures showed a large number of type II pneumococci in the blood. The serum from 24 of those who recovered protected mice against 100 lethal doses, while 3 others protected against 10 lethal doses of virulent pneumococci. Among the fatal cases, homologous protection against more than 10 lethal doses was not found and heterologous protection was never demonstrated. More recently, in a series reported by McLeod, Hoagland, and Beeson (12), of 13 cases who gave a positive skin reaction prior to serum treatment, all survived. It may, perhaps, be inferred from these 3 small series that for the most part the individual who recovers from pneumonia might be considered a good reactor, as indicated by the skin reaction and by the presence of serum antibodies.

Inasmuch as the pneumococcus is widespread in the general population, positive skin reactions should also occur in normal individuals not actively immunized. The observations on the cutaneous test of Francis and Tillett in normal individuals has been reported by Finland and Sutliff, Alston and Lowdon, and Rogers and Wagner. The first investigators tested only 24 individuals who had no recent history of pneumonia. Four of these (16.7 percent) responded against type I, and 10 (41.7 percent) against type II. Rogers and Wagner, using only type I carbohydrate, found that out of 78 persons tested 56, or 71.8 percent, gave a positive skin reaction. In a larger group, 281 persons, Alston and Lowdon observed skin reactions in 63 percent. They state, "In all groups 281 persons were tested, and 178 (63 percent) gave primary reactions exactly similar to those previously produced in pneumonia convalescents with the type I or type II carbohydrate." If from this number the 15 infants under 1½ years of age are deducted, then of the remaining 266, 178 (67 percent) gave positive reactions. The reports of skin tests on this group were for type II SSS only. From our observations 47 percent of 67 individuals gave positive skin tests with type I, and 11 percent of 63 with type II antigen. Inasmuch as pneumococci are almost universally present, the positive skin reactions might be inferred to occur only in individuals who respond readily to pneumococcus antigen. Such individuals may be classified as good reactors.

However, in the study of the comparison between skin reactions and serum antibodies, the correlation was of low degree. The errors are two: First, a positive skin reaction without serum antibody; and

second, a negative one in the presence of antibody. The total error was found to be 42 percent for type I and 40 percent for type II. On the other hand, after immunization of the group tested with the Francis-Tillett technique, the error in both type I and type II was 20 percent. But when the antigen-antibody complex in dilution of 1:100,000 was used as the skin test antigen in immunized individuals instead of the free SSS, this error was reduced to 5 percent with type I and 8 percent with type II. This reduction of the error in correlation between skin test and serum antibody titer, especially, in the case of the complex antigen after immunization, suggests a means of separating the good from the poor reactors.

The results with the immunizing antigen of pneumococcus used in our investigations indicate that for white mice the active polysaccharide contains practically all of the immunizing activity of the pneumococcus, as a matter of fact, many more immunizing doses as tested in white mice than calculated from the organisms from which it is derived (13). Moreover, this antigen stimulates demonstrable antibody production best in mice and man. Failure of response in man to a single injection of the antigen occurs in our series in from 2 to 4 percent. This may be due to an inherent characteristic of the individual or a transitory state of an inability to manufacture antibody. Indeed, proof is lacking as to whether the antigenic polysaccharide is the best immunizing agent for man against pneumococcus infection. This proof can be obtained only by comparing in human beings the effect of the original organisms and the various components isolated therefrom. Nevertheless, in the large proportion of individuals injected up to the present time, one injection of the antigen is as active as multiple injections of pneumococcus vaccine. Unfortunately, a study on whole-cell vaccine has not been made in relationship to individual response as measured by serum antibody content. As a matter of fact, vaccines have generally been used in man without proof of antigenicity even in the experimental animal, in the hope of increasing resistance to pneumococcus infections, truly an illogical and unscientific procedure. However, the issue at present is an attempt to measure individual susceptibility to pneumococcus infection.

This report, as well as previous ones, demonstrates the variability of response in humans to the antigenic polysaccharide of the pneumococcus as measured by serum antibody content. Individual variation in response to pneumococcus infection may also be inferred from the mortality rate in lobar pneumonia. For it has long been recognized, even before typing, that in the United States approximately 75 percent of pneumonia patients survive when nonspecific therapeutic measures are employed. In other words, the disease is self-limiting in 3 out of 4 patients. The question arises whether those who survive have either a possible unexplained natural resistance or a

special mechanism for the development of antibodies more readily than those who succumb to the infection. At least this latter assumption is open to experimental proof. For it is relatively simple to inject a large enough sample of the general population of different age groups, and skin test each 14 days afterwards, to divide the number into 2 groups according to the presence or absence of skin reaction. Without further tests, those injected in the 2 groups could be followed over a period of years, and the morbidity and mortality rate of pneumonia determined. If the assumption is correct that among those in the group who fail to react to the skin test the morbidity and mortality rates are high in comparison with the good reactors, then efforts could be directed toward prophylaxis in this relatively small percentage of the population with more assurance of successful results than in any attempt to immunize the general population. For, if, in a larger sample of the population, the reliability of the SSS-antibody complex is confirmed, only approximately 10 percent or less of the population would be considered susceptible. To obtain these facts, experiments carried out over a period of at least 3 years, or until serum antibodies produced by injection of the immunizing antigen are dissipated, would be necessary.

The above assumption leaves out of consideration nonspecific factors which may influence both morbidity and mortality rates in pneumonia. It is well known, from work on experimental animals, that heredity plays a part in resistance of animals to artificially induced infections. Other factors, such as environmental conditions, including geographical location, habits of life, diet, both organic and inorganic, undoubtedly have a bearing on the resistance of humans to infective agents. For a complete study looking towards the prophylaxis of pneumonia, all these elements must be taken into consideration. However, the present thesis is the possibility of separating the general population into 2 groups, good and poor reactors to a specific immunological agent, and of determining just how much the morbidity and mortality rates of lobar pneumonia vary in these 2 groups. It is an approach from the specific standpoint in contrast to methods of increasing general resistance to all infective agents.

SUMMARY AND CONCLUSIONS

Certain inferences may be drawn from this report on the correlation between cutaneous reactions and pneumococcus serum antibodies in man:

1. There was no quantitative relationship found between the intensity of the skin reactions of Francis and Tillett and serum antibody titer of individuals before or after immunization with antigenic polysaccharide of the pneumococcus.

2. Using the Francis and Tillett test as indicator, it was found that the group of individuals before immunization gave positive reactions to type I skin test antigen in 48 percent and after immunization in 84 percent of cases; with type II in 11 percent and 78 percent, respectively. As measured by the mouse protection test, only 2 percent failed to show protective antibodies in their sera.

3. The percentage of error, or lack of agreement, found between the results of the Francis and Tillett skin test and serum antibody titer for both type I and type II was 20 percent when lack of agreement included those with negative skin reaction and positive blood tests and those with positive skin and negative blood tests.

4. When the antigen-antibody complex in dilution of 1:100,000 is used as skin test antigen, a negative reaction (in contrast to the free antigen of Francis and Tillett) indicates the presence of serum antibodies. This test used in a group of 117 immunized individuals, gave in the case of type I an error of 5.1 percent and with type II, 7.7 percent. There is less discrepancy between skin test and presence of serum antibody in this group of individuals than found in the test with free SSS antigen.

5. A possibility has been suggested of measuring individual susceptibility of man to pneumococcus infections by first injecting an immunizing dose of the polysaccharide, and 14 days afterwards performing a skin test. An indication of immunity, in the case of the Francis-Tillett technique, is a positive skin reaction consisting of erythema and wheal. Conversely, a positive test for immunity with an appropriate dose of the antibody-antigen complex is a negative skin reaction similar to the Schick test in diphtheria when antitoxin is present. Such a procedure would separate individuals into good and poor reactors in view of determining the morbidity and mortality rates of lobar pneumonia in the two groups, as a guide for further study towards possible prophylaxis against pneumococcus infections with the active polysaccharide.

ACKNOWLEDGMENTS

We wish to express our appreciation to Dr. W. R. Cameron for aid in the field study and to Mr. J. W. Byron of the Byron Tanneries for his helpful cooperation. We are indebted to Miss Kathryn Donehoo and Miss Barbara Ottinger for technical assistance in running the mouse protection tests.

REFERENCES

- (1) Felton, L. D.: Studies on immunizing substances in pneumococci. VII. Response in human beings to antigenic pneumococcus polysaccharides, types I and II. *Pub. Health Rep.*, **53**: 1855 (1938).
- (2) Francis, T., and Tillett, W. S.: Cutaneous reactions in pneumonia. The development of antibodies following the intradermal injection of type-specific polysaccharide. *J. Exp. Med.*, **52**: 573 (1930).

- (3) Finland, M., and Sutliff, W. D.: Specific cutaneous reactions and circulating antibodies in the course of lobar pneumonia. I. Cases receiving no serum therapy. *J. Exp. Med.*, **54**: 637 (1931).
- (4) Finland, M., and Dowling, H. F.: Cutaneous reactions and antibody response to intracutaneous injections of pneumococcus polysaccharides. *J. Immunol.*, **29**: 285 (1935).
- (5) Heidelberger, M., Kendall, F. E., and Scherp, H. W.: The specific polysaccharides of types I, II, and III pneumococcus. A revision of methods and data. *J. Exp. Med.*, **64**: 559 (1936).
- (6) Sutliff, W. D., and Finland, M.: Antipneumococcic immunity reactions in individuals of different ages. *J. Exp. Med.*, **55**: 837 (1932).
- (7) Davies, J. A. V.: The response of infants to inoculation with type I pneumococcus carbohydrate. *J. Immunol.*, **33**: 1 (1937).
- (8) Alston, J. M., and Lowdon, A. S. R.: Studies of the skin reactions to the specific soluble substances of the pneumococcus types I and II. *Brit. J. Exp. Path.*, **14**: 1 (1933).
- (9) Heidelberger, M., and Avery, O. T.: The soluble specific substance of pneumococcus. *J. Exp. Med.*, **38**: 73 (1923).
- (10) Rogers, E. S., and Wagner, H. C.: Relation between skin reactions to specific carbohydrate type I pneumococcus and human blood groups. *Proc. Soc. Exp. Biol. and Med.*, **33**: 249 (1935).
- (11) Francis, T.: Antigenic action of the specific polysaccharide of pneumococcus type I in man. *Proc. Soc. Exp. Biol. and Med.*, **31**: 493 (1934).
- (12) McLeod, C., Hoagland, C., and Beeson, P.: The use of the skin test with the type specific polysaccharides in the control of serum dosage in pneumococcal pneumonia. *J. Clin. Invest.*, **17**: 739 (1938).
- (13) Felton, L. D., and Kauffmann, G.: Studies on immunizing substances in pneumococci. VI. The essential immunizing antigen of types I and II pneumococci. *Bull. Johns Hopkins Hosp.*, **62**: 430 (1938).

ROCKY MOUNTAIN SPOTTED FEVER

Protective Value for Guinea Pigs of Vaccine Prepared from *Rickettsiae* Cultivated in Embryonic Chick Tissues¹

By HERALD R. COX, *Associate Bacteriologist, Rocky Mountain Laboratory, United States Public Health Service*

A simplified technique whereby the yolk sac of the developing chick embryo may be used for the cultivation of rickettsiae of the Rocky Mountain spotted fever and typhus groups has recently been reported by the writer (1). It has since been determined that vaccines prepared from rickettsiae grown in chick embryonic tissues can be successfully used for the active immunization of guinea pigs against Rocky Mountain spotted fever.

MATERIALS AND METHODS

The material used for the preparation of vaccine was the pooled embryonic tissues (yolk sac, chorioallantois, and embryo) from passage eggs of a western Montana strain of Rocky Mountain spotted fever (series B of the preceding paper (1)). In previous experiments (1) it was shown that the yolk sac has a higher limit of infectivity than other tissues of the developing chick. The other tissues, however,

¹ From the Division of Infectious Diseases, National Institute of Health, Rocky Mountain Laboratory, Hamilton, Mont.

contain a fairly large number of rickettsiae, and in this series of tests all the embryonic tissues were used.

Before inoculation the eggs were incubated 5 to 10 days at 39° C. The inoculum, 0.5 cc. of a 10-percent yolk-sac suspension in saline, was injected into the yolk by means of a 1¼-inch, 21-gage needle introduced through the air sac end of the egg. The eggs were then placed in a 35° C. incubator until death of the embryo, which invariably occurred in 3 or 4 days. In a few instances incubation at this temperature was continued for a day longer. In either case the eggs were then transferred to room temperatures for periods of 2 to 12 days before use for vaccine preparation.

Preparation of vaccine.—The embryonic tissues were completely removed aseptically from a number of eggs of the same transfer and washed once or twice with sterile saline to remove any yolk or other fluids that might be present. They were then drained free from excess moisture, pooled, weighed, and ground with sterile alundum to a homogeneous suspension. Sterile saline was added to make a 2- or 3-percent suspension. A portion of the suspension was reserved for titration and to the remainder was added phenol to 0.4 and formalin to 0.1 percent concentration. The suspension was then stored at 2° C. and subjected to daily shaking for 6 or 7 days. In 12 or 14 days it was centrifuged at 2,500 to 3,000 revolutions per minute for 20 minutes, except for vaccine 39-2. (See table 1.²) The supernatant fluid thus obtained was used as vaccine.

TITRATION TESTS FOR INFECTIVITY OF EMBRYONIC TISSUE SUSPENSIONS

Titration was made to determine the infective titer of the various suspensions used and to see whether differences found in immunizing powers might be related to the number of infectious doses in the source material. The titer was determined as follows:

The suspension was centrifuged (2,000 to 2,500 revolutions per minute for 15 minutes) to throw down tissue fragments. The supernatant fluid was pipetted off, tenfold dilutions were prepared with ascitic fluid or with a mixture containing equal volumes of ascitic fluid and Tyrode's solution, and each dilution was tested by injecting guinea pigs intraperitoneally with 1 cc. each. Animals that survived or that failed to show the characteristic scrotal reaction were later tested against infectious guinea pig blood.

Vaccine tests.—Guinea pigs received subcutaneously either one 1-cc. dose of vaccine or two 1-cc. doses given 6 or 7 days apart. In one test only a single injection of 0.5 cc. of vaccine was used (experiment 3). Temperatures were taken daily throughout the period of immunization as well as through the period following the test for immunity.

² An angle centrifuge was used in all experiments.

Twelve to sixteen days after the last injection of vaccine the animals were tested for immunity by injecting each intraperitoneally with 1 cc. of a pooled mixture of citrated whole blood taken from infected guinea pigs on the third or fourth day of fever. Six normal, control guinea pigs received the same inoculum, except that 10 were used in experiment 3. In addition, decimal dilutions (10^{-1} , 10^{-2} , 10^{-3} , 10^{-4}) of the blood were tested in other control guinea pigs so as to determine the approximate number of infectious doses given the vaccinated guinea pigs.

EXPERIMENTAL DATA

Twelve lots of vaccine were prepared and tested. Two lots (39-1 and 39-2) were tested three times, three twice (41, 43, and 44), and the remaining seven, once.

Table 1 presents the data pertaining to the preparation of the various lots.

TABLE 1.—Preparation data for lots of spotted fever vaccines made from the embryonic tissues of developing chicks. The lot number represents the number of the serial passage of the spotted fever strain in eggs at the time the vaccine was prepared

Vaccine No.	Date of preparation	Number of embryos and age when inoculated	Number of days eggs were kept at 35° C. and room temperature before being used		Concentration of tissue in crude vaccine suspension	Approximate infectivity end-point of tissues
			At 35° C.	At room temperature		
39-1	1938 Oct. 8	8-5 days	4	3	3×10^{-1}	3×10^{-1}
39-2 ¹	do.				3×10^{-1}	
41	Oct. 25	1-5 day; 1-6 day; 1-7 day; 1-8 day	4	12	3×10^{-1}	3×10^{-4}
43	Oct. 26	4-6 days	4	4	3×10^{-1}	3×10^{-4}
44	Nov. 4	do.	4	8	3×10^{-1}	3×10^{-4}
52	Dec. 10	do.	3	4	3×10^{-1}	3×10^{-7}
54	Dec. 13	do.	4	4	2×10^{-1}	2×10^{-4}
55	Dec. 15	4-7 days	4	2	2×10^{-1}	2×10^{-4}
56-1	Dec. 20	4-6 days	3	3	2×10^{-1}	2×10^{-4}
56-2	do.	2-7 days	3	3	2×10^{-1}	2×10^{-4}
56-3	do.	2-8 days	3	3	2×10^{-1}	2×10^{-4}
56-4	do.	2-10 days	3	3	2×10^{-1}	2×10^{-4}

¹ Vaccine lot 39-2 was prepared by centrifuging 180 cc. of lot 39-1 at 5,500 revolutions per minute for 1 hour. The precipitate thus obtained, resuspended in $\frac{1}{10}$ the original volume (18 cc. of saline containing 0.1 percent formalin and 0.4 percent phenol) constituted lot 39-2.

² 3×10^{-1} = 3 percent; 2×10^{-1} = 2 percent.

These data show that the infectivity end-point per gram of embryonic tissues varied considerably. Vaccines 41, 54, and 56-3 showed the lowest number of infectious doses (3,000 to 5,000) while vaccine 52, containing at least 3 million infectious doses, showed the highest number. The small number of vaccine lots tested shows no apparent correlation between the infective titer and the length of time the eggs were allowed to stand at incubator and room temperatures.

Experiment 1.—The first test was made with vaccine lots 39-1 and 39-2. On October 20, 1938 (12 days after preparation), six guinea pigs received 1 cc. each of lot 39-1 and six others 1 cc. each of lot 39-2. All remained afebrile. The test for immunity was given 12 days later. Ten of the twelve vaccinated animals showed no temperature rise, while two (one for each lot of vaccine) had low fevers for 3 or 4 days, respectively. No scrotal swelling or other evidence of spotted fever was observed in the vaccinated animals. The six controls injected with the undiluted infectious blood as well as those receiving the 10^{-1} and 10^{-2} dilutions developed typical spotted fever; six died. The controls receiving the 10^{-3} and 10^{-4} dilutions of blood failed to react and were later shown to be nonimmune.

No differences were detected in the protective properties of the two vaccines, although lot 39-2 was prepared by concentrating lot 39-1 tenfold.

TABLE 2.—Daily temperature records ($^{\circ}$ C.) of vaccinated guinea pigs used in experiment 1, vaccine lots 39-1 and 39-2

Oct. 20, 1938¹.—Guinea pigs were each injected subcutaneously with 1 cc. of vaccine.

Nov. 1, 1938.—Guinea pigs were each injected intraperitoneally with 1 cc. of infectious blood.

Guinea pig No.	Lot 39-1						Lot 39-2					
	1	2	3	4	5	6	7	8	9	10	11	12
Nov. 2, 1938.....	39.3	39.0	39.0	39.0	38.5	39.0	38.5	39.2	39.0	39.0	39.0	38.6
Nov. 3, 1938.....	39.0	38.5	39.2	39.0	38.5	39.0	38.0	38.8	39.0	38.7	39.0	38.8
Nov. 4, 1938.....	39.0	38.7	38.5	39.2	38.8	38.8	39.2	39.0	39.0	38.9	39.3	38.7
Nov. 5, 1938.....	39.0	38.3	39.4	38.4	39.4	39.0	39.4	39.0	39.2	38.8	39.0	39.0
Nov. 6, 1938.....	39.2	39.0	39.3	38.6	39.0	39.8	39.4	39.6	39.8	39.0	38.8	39.0
Nov. 7, 1938.....	39.4	39.4	39.0	38.8	38.5	40.0	38.7	39.0	39.8	38.8	38.9	39.0
Nov. 8, 1938.....	39.0	39.0	39.5	39.0	38.8	40.3	38.8	39.1	39.4	38.6	38.4	38.8
Nov. 9, 1938.....	39.4	38.6	39.0	39.0	38.7	39.7	39.3	39.2	39.5	38.8	38.8	39.0
Nov. 10, 1938.....	39.4	38.6	39.1	38.8	38.8	39.0	39.1	38.8	39.5	38.8	39.0	38.8
Nov. 11, 1938.....	39.2	39.1	39.2	39.0	39.0	39.2	39.0	38.6	39.5	38.6	38.8	38.5
Nov. 12, 1938.....	38.8	39.4	39.2	39.0	39.0	39.4	39.2	38.8	39.0	38.8	39.0	38.5
Nov. 13, 1938.....	39.2	39.0	38.6	39.0	38.5	39.2	39.3	39.2	39.4	38.5	38.5	38.8
Nov. 14, 1938.....	39.4	39.2	38.8	39.3	38.5	38.8	39.4	39.4	39.0	38.8	39.2	38.8
Nov. 15, 1938.....	39.4	39.1	38.8	39.4	38.8	39.1	39.0	39.0	39.0	39.0	38.6	38.8
Nov. 16, 1938.....	39.4	39.0	39.1	39.0	39.0	39.4	39.2	38.8	38.8	38.8	38.6	38.6

¹None of the vaccinated guinea pigs showed any thermal reaction due to the injection of vaccine.

Tables 2 and 2a show the temperature records of the vaccinated and control guinea pigs.

Experiment 2.—The second test was made with the two vaccine lots used in experiment 1 plus three additional lots (41, 43, and 44). Six animals were used for each lot, and on November 30, 1938, each received 1 cc. of vaccine. The immunity test was given 16 days later.

Of the six animals vaccinated with lot 39-1, none showed scrotal swelling, but one had temperatures of 40.3° , 39.7° , and 39.7° C. on the seventh, eighth, and ninth days, respectively.

Five of the guinea pigs that received lot 39-2 showed no reaction. The sixth died of pneumonia on the second day after being tested for immunity.

TABLE 2a.—Daily temperature records (°C.) of control guinea pigs used in experiment 1

November 1, 1938.—Guinea pigs were injected intraperitoneally with 1 cc. each of infectious blood.

Guinea pig No.-----	Undiluted blood						Blood dilution							
							10 ⁻¹		10 ⁻²		10 ⁻³		10 ⁻⁴	
	13	14	15	16	17	18	19	20	21	22	23	24	25	26
Nov. 2, 1938..	39.0	38.6	38.8	39.0	38.8	39.0	38.4	38.5	38.8	38.8	38.7	39.0	39.2	39.0
Nov. 3, 1938..	39.0	39.0	38.8	39.2	39.0	39.4	39.0	39.0	39.0	39.2	38.8	38.8	38.8	38.8
Nov. 4, 1938..	39.4	39.2	39.0	38.4	39.4	39.0	39.0	39.4	39.0	39.2	39.0	39.0	39.1	38.8
Nov. 5, 1938..	40.2	39.8	40.4	40.0	40.6	39.2	39.0	39.0	39.0	39.4	39.2	39.0	38.8	39.0
Nov. 6, 1938..	40.2	40.4	40.0	40.2	40.7	40.4	40.3	39.5	39.5	39.6	39.2	39.2	39.0	39.2
Nov. 7, 1938..	41.0	40.7	40.6	40.6	40.8	40.2	39.8	41.0	40.0	40.4	39.2	39.2	39.0	39.0
	SS	SS	SS		SS									
Nov. 8, 1938..	40.8	40.4	41.0	40.4	40.2	41.0	39.8	41.0	39.9	40.8	39.0	39.0	39.0	38.8
	SS	SS	SS	SS	SS									
Nov. 9, 1938..	40.8	40.8	41.0	40.8	39.2	40.8	40.3	41.3	40.3	40.4	39.4	38.6	39.2	39.0
	SH	SH	SH	SS	SS	SS	SS	SS						
Nov. 10, 1938..	40.7	40.8	41.0	40.4	37.0	40.6	40.5	41.5	40.4	40.6	38.6	38.8	39.4	39.0
	SH	SH	SN	SS		SH	SS	SS	SS	SS				
Nov. 11, 1938..	40.0	40.6	37.0	40.0	D	40.2	40.0	40.8	40.5	40.0	38.8	39.0	38.8	39.0
	SN	SH	SN	SS		SH	SS	SH	SS	SS				
Nov. 12, 1938..	39.0	37.2	D	40.0	-----	38.2	40.3	40.8	40.5	40.0	38.0	39.2	38.8	38.8
	SN	SN		SS		SH	SS	SH	SS					
Nov. 13, 1938..	37.0	D	-----	39.6	-----	D	39.4	40.6	40.2	39.8	38.6	39.0	38.6	39.0
	SN			SS				SN	SS					
Nov. 14, 1938..	D	-----	-----	39.4	-----	-----	39.2	40.4	40.4	39.6	39.0	39.4	38.4	39.2
								SN	SS					
Nov. 15, 1938..	-----	-----	-----	39.2	-----	-----	39.0	39.0	40.2	39.2	39.2	39.2	38.6	39.0
								SN	SS					
Nov. 16, 1938..	-----	-----	-----	39.0	-----	-----	39.0	D	39.8	39.2	39.0	39.0	38.8	39.0
				S			S		SS	S	S	S	S	S

SS—scrotal swelling.

SH—scrotal hemorrhage.

SN—scrotal necrosis and slough.

S—survived.

D—died.

Of the six that received lot 43, five remained afebrile. The sixth showed a temperature of 40° C. on the eighth and ninth days, but no scrotal reaction.

The six control animals injected with the undiluted blood, as well as the six that received the 10⁻¹, 10⁻², and 10⁻³ dilutions, all developed typical spotted fever. Seven died. Those receiving the 10⁻⁴ dilution remained afebrile.

The results obtained with vaccines 41 and 44 were not significant. Nine of the twelve records were invalidated by concurrent pneumonia. The three remaining guinea pigs (one of lot 41 and two of lot 44) remained afebrile following both the vaccine injection and the immunity test.

Experiment 3.—The third test was carried out with the five vaccine lots used in experiment 2 plus seven additional lots (52, 54, 55, 56-1, 56-2, 56-3, and 56-4). The immunization procedure varied somewhat from that used previously. The guinea pigs injected with lot 39-2 received only 0.5 cc. (January 4, 1939), and two series of test

animals were used for each of lots 41, 43, 44, 52, 54, 55, 56-1, 56-2, 56-3, and 56-4. One series received a single injection of 1 cc. (January 4, 1939), while the second received two 1-cc. injections 6 days apart (January 4 and 10). The immunity test was given all animals on January 24. In this experiment 10 control animals received the 1-cc. injections of undiluted infectious blood. The data are summarized in table 3.

TABLE 3.—*Test of vaccinated guinea pigs for protection against Rocky Mountain spotted fever*

Immunization			Test for immunity							
Vaccine Lot No.	Age of vaccine (days)	Dosage	Dilution of blood	Number showing fever of 39.8° C. or above			Number showing scrotal swelling	Number fully protected	Number showing typical spotted fever	Number dying of spotted fever
				1 day	2 days	More than 2 days				
39-1	94	1 cc.	Undiluted	0 of 6	0 of 6	0 of 6	0	6 of 6	0	0
39-2	94	0.5 cc.	do.	0 of 6	0 of 6	0 of 6	0	6 of 6	0	0
41	77	1 cc.	do.	0 of 6	0 of 6	0 of 6	0	6 of 6	0	0
41	71	1 cc. twice	do.	0 of 6	0 of 6	0 of 6	0	6 of 6	0	0
43	76	1 cc.	do.	0 of 6	0 of 6	0 of 6	0	6 of 6	0	0
43	70	1 cc. twice	do.	0 of 6	0 of 6	0 of 6	0	6 of 6	0	0
44	67	1 cc.	do.	1 of 4 ¹	0 of 4	0 of 4	0	3 of 4	0	0
44	61	1 cc. twice	do.	1 of 6	0 of 6	0 of 6	0	5 of 6	0	0
52	31	1 cc.	do.	0 of 6	0 of 6	0 of 6	0	6 of 6	0	0
52	25	1 cc. twice	do.	0 of 6	0 of 6	0 of 6	0	6 of 6	0	0
54	28	1 cc.	do.	1 of 6	1 of 6	0 of 6	0	4 of 6	0	0
54	22	1 cc. twice	do.	1 of 5 ¹	0 of 5	0 of 5	0	4 of 5	0	0
55	26	1 cc.	do.	0 of 6	0 of 6	0 of 6	0	6 of 6	0	0
55	20	1 cc. twice	do.	0 of 6	0 of 6	0 of 6	0	6 of 6	0	0
56-1	21	1 cc.	do.	0 of 6	0 of 6	0 of 6	0	6 of 6	0	0
56-1	15	1 cc. twice	do.	1 of 6	0 of 6	0 of 6	0	5 of 6	0	0
56-2	21	1 cc.	do.	0 of 6	0 of 6	0 of 6	0	6 of 6	0	0
56-2	15	1 cc. twice	do.	0 of 6	0 of 6	0 of 6	0	6 of 6	0	0
56-3	21	1 cc.	do.	2 of 6	0 of 6	0 of 6	0	4 of 6	0	0
56-3	15	1 cc. twice	do.	1 of 6	0 of 6	0 of 6	0	5 of 6	0	0
56-4	21	1 cc.	do.	0 of 6	0 of 6	0 of 6	0	6 of 6	0	0
56-4	15	1 cc. twice	do.	1 of 6	0 of 6	0 of 6	0	5 of 6	0	0
			Undiluted			10 of 10	10 of 10		10 of 10	7 of 10
			10 ⁻¹			2 of 2	2 of 2		2 of 2	1 of 2
			10 ⁻²			1 of 2	1 of 2		1 of 2	0 of 2
			10 ⁻³			0 of 2	0 of 2		0 of 2	0 of 2
			10 ⁻⁴			0 of 2	0 of 2		0 of 2	0 of 2
Controls										

¹ 2 animals of the lot 44 series and 1 animal of the lot 54 series died of intercurrent infection before being given the immunity test.

The table shows that all 12 vaccines were potent and complete protection was apparently afforded to 119 of the 129 vaccinated guinea pigs (valueless animals excluded). Of the 10 animals that had 1 or 2 days of low fever, none showed scrotal swelling or noticeable evidence of illness. Two of the vaccines, 39-1 and 39-2, had been stored in the cold for 94 days. There was no apparent loss of potency. Moreover, a single injection of 0.5 cc. of vaccine 39-2 afforded complete protection.

It is of interest that infected eggs held at room temperature for as long as 12 days (see lot 41, table 1) yielded potent vaccine.

DISCUSSION

It has been conclusively established by a number of investigators that active immunity against rickettsial infections can be induced by vaccination with killed rickettsiae. In the case of Rocky Mountain spotted fever, the vaccine of Spencer and Parker (2), produced from infected ticks (*Dermacentor andersoni*) has unquestionably been of great value. However, the method of preparation is exceedingly tedious and workers are necessarily exposed in an unusual degree to an ever-present danger of infection.

In 1937 Bengtson (3) reported successful immunization of guinea pigs against spotted fever with formolized rickettsial suspensions prepared from infected guinea pig tissues cultivated by a modified Maitland method. By this method the amount of vaccine obtained from the tissues of one guinea pig was sufficient to immunize 40 or 50 guinea pigs against the usual test dose.

In unpublished experiments the writer also has successfully used modified Maitland cultures in carrying 6 series of Rocky Mountain spotted fever cultures through more than 30 serial transplants each. The cultures were prepared by suspending minced chick-embryo tissue in filtered human ascitic fluid.³ Moderately good growths of rickettsiae were obtained under these conditions, but attempts to increase the yield by substituting *chorio-allantoic membrane* of chick embryos and guinea pig tunicae for the minced chick embryo and by using various modifications of Baker's solution (4) (horse, cow, guinea pig, rabbit, and chicken sera, as well as human amniotic and ascitic fluids and filtered extracts of normal tick tissues (*Dermacentor andersoni*)) were not particularly successful. While several potent lots of vaccine were made from the various modified Maitland cultures, none of the cultural variations seemed satisfactory for the preparation of vaccine of consistent potency. Moreover, as Zinsser and his colleagues have recently pointed out (5), the Maitland method, because of certain technical difficulties, does not appear to be readily applicable to large-scale production.

The method described in this paper has thus far produced consistently good vaccines. Furthermore, from the standpoints of potential cost, ease of manipulation, and quantity production, it has given results that we have been unable to approach by any other method. Thus, 320 cc. of vaccine 56-2 was prepared from two embryos 7 days

³ In a similar manner Greek and Moroccan strains of boutonneuse fever were each carried through 20 passages, a strain of exanthematic typhus of Sao Paulo (Brazilian spotted fever) through 15, 2 strains of endemic typhus through 16 and 26, respectively, and a strain of European (epidemic) typhus through 14. However, attempts to grow these rickettsiae in cultures consisting of minced chick-embryo tissue suspended in Tyrode's solution (0.5 gram NaHCO₃ per liter) either ended in failure or gave very scanty growth. Somewhat better results were obtained when sera (20 to 40 percent) were added to Tyrode's and the results were still better when various modifications of Baker's solution were used. However, the results were best and most consistent when the suspension medium was filtered human ascitic fluid.

old at the time of inoculation. Even more striking is the fact that 1,080 cc. of vaccine 56-4 was made from two 10-day-old embryos. A single 1 cc. injection of either vaccine was sufficient to protect a guinea pig against the usual test dose of infectious blood. On the basis of the dosage of tick-tissue vaccine now used for human prophylaxis (two injections of 2 cc. each) the amount of vaccine obtained from the two 10-day-old embryos would be sufficient to immunize 270 persons.

CONCLUSION

Vaccine which will protect guinea pigs against Rocky Mountain spotted fever can be prepared from infected embryonic tissues of developing chicks.

REFERENCES

- (1) Cox, H. R.: Use of yolk sac of developing chick embryo as medium for growing rickettsiae of Rocky Mountain spotted fever and typhus groups. Pub. Health Rep., **53**: 2241 (1938).
- (2) Spencer, R. R. and Parker R. R.: Studies on Rocky Mountain spotted fever. Hyg. Lab. Bull. No. 154, 1930. Page 63.
- (3) Bengtson, Ida A.: Immunizing properties of formolized Rocky Mountain spotted fever rickettsiae cultivated in modified Maitland media. Pub. Health Rep., **52**: 1696 (1937).
- (4) Baker, Lillian E.: Artificial media for the cultivation of fibroblasts, epithelial cells and monocytes. Science, **83**: 605 (1936).
- (5) Zinsser, H., Fitzpatrick, F., and Wei, H.: A study of rickettsiae grown on agar-tissue cultures. J. Exp. Med., **69**: 179 (1939).

THE PRESERVATION OF LYMPHOCYTIC CHORIOMENINGITIS AND ST. LOUIS ENCEPHALITIS VIRUSES BY FREEZING AND DRYING *IN VACUO*¹

By JERALD G. WOOLEY, *Bacteriologist, United States Public Health Service*

The maintenance of the viruses of lymphocytic choriomeningitis and encephalitis, St. Louis type, is usually accomplished by serial inoculations of animals and the recovery of tissues that are known to contain a high concentration of the virus, by virus cultures in chick embryos, or by virus tissue cultures. These methods are expensive and time consuming; also the viruses may change certain of their pathogenic traits or become "fixed" or capable of attacking only certain tissues.

A procedure for preserving sera, solutions, cultures, and the like, by freezing and drying *in vacuo* was described by Florsdorf and Mudd (1). By a modification of the technique described by these authors, a method has been worked out whereby these viruses have been preserved in a dry state. Also, the original characteristics of one of the dried viruses (the Green strain of lymphocytic choriomeningitis

¹ From the Division of Infectious Diseases, National Institute of Health, Washington, D. C.

virus) has been maintained, whereas by serial intracerebral transfer in white mice this strain of virus had become fixed for mouse brain tissue.

TECHNIQUE

Pieces of virus-bearing tissue that have been freshly removed are utilized. A piece of tissue, 0.3 to 0.5 gm., is placed in the bottom of a sterile pyrex test tube at least 15 mm. in diameter. The test tube is then quickly heated about 7.5 cm. from the bottom by a blast burner with a narrow flame and drawn out to a diameter of approximately 4 to 6 mm. (care must be taken that the bottom of the test tube is kept cool). The tube is then connected by means of a rubber stopper, rubber pressure tubing, and glass tubing to the manifold of the Flosdorf-Mudd apparatus. After the machine is ready for operation, the end of the tube containing the tissue is immersed in a tray of methyl cellosolve and cracked, solid carbon dioxide. After about 10 minutes, when the tissue is frozen, a vacuum of at least 0.05 mm. of mercury is induced and maintained throughout the process of drying. The end of the tube containing the virus-bearing material is kept submerged in the carbon dioxide-methyl cellosolve mixture. Cracked carbon dioxide is added to the trays at frequent intervals for 8 hours, thus keeping the temperature at about -75°C . After this time no more carbon dioxide is added and the solution in the trays slowly returns to room temperature. When the vacuum has been maintained for 22 to 24 hours, the constricted portion of the test tube is sealed off with a flame. The vacuum should be maintained until all tubes are sealed. The ampules are stored in a cold room at about 5°C .

Tested by animal inoculation lymphocytic choriomeningitis virus remained viable after 153, 260, and 378 days. Dried encephalitis (St. Louis type) virus remained viable after 361 and 833 days in storage (table 1). No failures to recover the virus in susceptible animals have resulted after preservation by this method.

TABLE 1.—Retention of potency by virus dried in vacuo

Virus-bearing tissue, dried	Date dried	Number of days storage to test	Date dried virus was inoculated into animals	Animals employed and route of inoculation	Results
Lymphocytic choriomeningitis infected mouse brain.	Apr. 24, 1937	153	Sept. 24, 1937	Mice IC....	Virus recovered.
Do.....	Sept. 11, 1936	378do.....do.....	Do.
Lymphocytic choriomeningitis infected monkey liver, kidney, and spleen.	Apr. 28, 1937	260	Jan. 13, 1937	Monkey IC, Sub Q and IP.	Do.
Encephalitis, St. Louis type, infected mouse brains.	Sept. 28, 1936	361	Sept. 24, 1937	Mice IC....	Do.
Do.....	Sept. 10, 1936	833	Dec. 22, 1938do.....	Do.

IC = Intracerebral.
Sub Q = Subcutaneous.
IP = Intraperitoneal.

SUMMARY

A method of freezing and drying is described by which the viruses of lymphocytic choriomeningitis and St. Louis encephalitis have been preserved for 378 and 833 days, respectively. Tests were not made at longer periods.

REFERENCE

- (1) Flosdorf, Earl W., and Mudd, Stuart: Procedure and apparatus for preservation in "lyophile" form of serum and other biological substances. *J. Immunol.* **29**: 389-425 (November 1935).

DEATHS DURING WEEK ENDED MAY 27, 1939

[From the Weekly Health Index, issued by the Bureau of the Census, Department of Commerce]

	Week ended May 27, 1939	Correspond- ing week, 1938
Data from 88 large cities of the United States:		
Total deaths.....	8,019	¹ 8,130
Average for 3 prior years.....	² 8,122	-----
Total deaths, first 21 weeks of year.....	191,399	183,351
Deaths under 1 year of age.....	471	¹ 495
Average for 3 prior years.....	² 517	-----
Deaths under 1 year of age, first 21 weeks of year.....	11,185	11,320
Data from industrial insurance companies:		
Policies in force.....	67,344,634	68,308,527
Number of death claims.....	12,689	12,038
Death claims per 1,000 policies in force, annual rate.....	9.8	9.2
Death claims per 1,000 policies, first 21 weeks of year, annual rate.....	11.6	9.9

¹ Data for 87 cities.

² Data for 86 cities.

PREVALENCE OF DISEASE

No health department, State or local, can effectively prevent or control disease without knowledge of when, where, and under what conditions cases are occurring

UNITED STATES

CURRENT WEEKLY STATE REPORTS

These reports are preliminary, and the figures are subject to change when later returns are received by the State health officers.

In these and the following tables, a zero (0) indicates a positive report and has the same significance as any other figure, while leaders (....) represent no report, with the implication that cases or deaths may have occurred but were not reported to the State health officer.

Cases of certain diseases reported by telegraph by State health officers for the week ended June 3, 1939, rates per 100,000 population (annual basis), and comparison with corresponding week of 1938 and 5-year median

Division and State	Diphtheria				Influenza				Measles			
	June 3, 1939, rate	June 3, 1939, cases	June 4, 1938, cases	1934-38, median	June 3, 1939, rate	June 3, 1939, cases	June 4, 1938, cases	1934-38, median	June 3, 1939, rate	June 3, 1939, cases	June 4, 1938, cases	1934-38, median
NEW ENG.												
Maine.....	0	0	0	0	422	70	105	105
New Hampshire.....	0	0	0	0	51	5	83	83
Vermont.....	0	0	0	0	1,743	130	79	39
Massachusetts.....	2	2	2	5	1,148	976	430	647
Rhode Island.....	0	0	0	0	1,038	136	7	40
Connecticut.....	0	0	0	2	3	1	3	1	1,718	579	97	183
MID. ATL.												
New York ¹	8	20	17	35	14	16	12	14	861	2,150	3,498	2,430
New Jersey ²	14	12	7	9	5	5	43	36	724	724
Pennsylvania ³	9	17	33	27	44	87	1,846	2,058
E. NO. CEN.												
Ohio ¹	12	15	21	27	10	13	22	74	96	1,491	2,038
Indiana.....	6	4	25	7	1	1	6	14	15	10	442	442
Illinois.....	15	23	31	32	5	8	14	15	23	35	1,059	1,059
Michigan ⁴	8	8	6	7	4	4	2	426	403	2,780	421
Wisconsin.....	4	2	3	3	62	35	27	24	1,306	743	2,703	1,481
W. NO. CEN.												
Minnesota.....	4	2	4	6	4	2	1	419	216	375	279
Iowa ¹	6	3	2	2	4	2	4	1	381	188	274	204
Missouri.....	4	3	11	15	6	36	5	4	137	137
North Dakota.....	0	0	0	0	343	47	6	5	102	14	67	47
South Dakota.....	0	0	1	1	60	8	1,473	196	4
Nebraska.....	0	0	4	2	23	6	611	160	252	90
Kansas.....	0	0	3	3	14	5	162	58	383	383

See footnotes at end of table.

Cases of certain diseases reported by telegraph by State health officers for the week ended June 3, 1939, rates per 100,000 population (annual basis), and comparison with corresponding week of 1938 and 5-year median—Continued

Division and State	Diphtheria				Influenza				Measles			
	June 3, 1939, rate	June 3, 1939, cases	June 4, 1938, cases	1934-38, median	June 3, 1939, rate	June 3, 1939, cases	June 4, 1938, cases	1934-38, median	June 3, 1939, rate	June 3, 1939, cases	June 4, 1938, cases	1934-38, median
SO. ATL.												
Delaware.....	0	0	0	0					708	36	7	17
Maryland ¹	6	2	1	4	19	6	2	2	398	129	16	259
Dist. of Col. ²	32	4	6	9			2	1	2,700	334	44	44
Virginia ³	28	15	5	9	163	87			1,872	999	607	380
West Virginia.....	19	7	4	7	11	4	27	11	19	7	339	161
North Carolina.....	10	7	7	7	1	1	1	2	671	459	948	309
South Carolina.....	8	3	2	2	514	188	77	77	41	15	128	65
Georgia ⁴	12	7	3	2	85	51			176	106	153	
Florida ⁵	9	3	7	7	54	18	1	1	220	73	44	20
E. SO. CEN.												
Kentucky.....	7	4	10	6	3	2	3	5	19	11	126	126
Tennessee ¹	5	3	1	4	35	20	18	18	145	82	104	104
Alabama ²	5	3	6	10	56	32	9	18	260	148	176	103
Mississippi ³	20	8	3	3								
W. SO. CEN.												
Arkansas.....	5	2	3	3	119	48	8	12	69	28	180	19
Louisiana.....	24	10	4	8	10	4	4	5	191	79	27	32
Oklahoma.....	4	2	9	8	44	22	25	25	322	160	171	49
Texas ¹	8	10	35	32	71	86	181	156	348	420	176	280
MOUNTAIN												
Montana.....	0	0	1	0	28	3			1,161	124	90	25
Idaho ¹	10	1	1	0					561	55	7	11
Wyoming ²	22	1	1	0					567	26	16	16
Colorado ³	29	6	18	5	34	7			727	151	178	178
New Mexico.....	0	0	1	2	12	1		1	173	14	16	52
Arizona.....	0	0	2	2	331	27	21	21	159	13	16	33
Utah ⁴	20	2	0	0	10	1			854	86	344	31
PACIFIC												
Washington.....	15	5	0	0					2,396	777	20	192
Oregon ¹	0	0	2	1	119	24	27	11	368	74	54	54
California ²	16	20	37	25	28	34	11	27	1,710	2,085	624	624
Total.....	9	236	339	353	38	804	490	552	517	12,783	21,443	21,443
22 weeks.....	17	9,267	11,032	11,692	315	147,113	41,924	100,639	553	301,185	682,231	582,885

Division and State	Meningitis, meningococcus				Pollomyelitis				Scarlet fever			
	June 3, 1939, rate	June 3, 1939, cases	June 4, 1938, cases	1934-38, median	June 3, 1939, rate	June 3, 1939, cases	June 4, 1938, cases	1934-38, median	June 3, 1939, rate	June 3, 1939, cases	June 4, 1938, cases	1934-38, median
NEW ENG.												
Maine.....	0	0	0	1	0	0	0	0	24	4	8	10
New Hampshire.....	0	0	0	0	0	0	0	0	51	5	22	20
Vermont.....	0	0	0	0	0	0	1	0	161	12	9	6
Massachusetts.....	2.4	2	1	3	0	0	0	0	162	138	326	230
Rhode Island.....	0	0	0	0	0	0	0	0	61	8	26	23
Connecticut.....	0	0	0	0	3	1	0	0	104	35	73	73
MID. ATL.												
New York ¹	2	5	1	6	0.8	2	0	1	145	362	519	610
New Jersey ²	2.4	2	0	1	1.2	1	0	0	142	119	97	133
Pennsylvania ³	9	18	3	8	0	0	0	0	98	194	292	342

See footnotes at end of table.

Cases of certain diseases reported by telegraph by State health officers for the week ended June 3, 1939, rates per 100,000 population (annual basis), and comparison with corresponding week of 1938 and 5-year median—Continued

Division and State	Meningitis, meningo-coccus				Poliomyelitis				Scarlet fever			
	June 3, 1939, rate	June 3, 1939, cases	June 4, 1938, cases	1934-38, median	June 3, 1939, rate	June 3, 1939, cases	June 4, 1938, cases	1934-38, median	June 3, 1939, rate	June 3, 1939, cases	June 4, 1938, cases	1934-38, median
E. NO. CEN.												
Ohio ²	2.3	3	5	5	0	0	0	0	205	267	182	508
Indiana.....	0	0	0	1	0	0	0	0	116	78	75	88
Illinois.....	2.6	4	3	5	1.3	2	0	0	182	277	320	412
Michigan ⁴	0	0	2	2	0	0	0	0	277	262	271	287
Wisconsin.....	0	0	1	0	1.8	1	2	0	181	103	144	263
W. NO. CEN.												
Minnesota.....	0	0	0	1	0	0	0	0	136	70	78	117
Iowa ²	2	1	0	0	0	0	0	1	91	45	64	68
Missouri.....	0	0	3	3	0	0	0	0	53	41	154	91
North Dakota.....	0	0	1	0	0	0	0	0	15	2	33	33
South Dakota.....	0	0	1	0	0	0	0	0	113	15	4	12
Nebraska.....	0	0	1	0	0	0	0	0	15	4	14	38
Kansas.....	0	0	0	0	0	0	0	0	106	38	57	57
SO. ATL.												
Delaware.....	0	0	0	0	0	0	0	0	98	5	3	2
Maryland ²	3	1	0	0	0	0	0	0	46	15	48	43
Dist. of Col. ²	0	0	2	2	0	0	0	0	57	7	11	11
Virginia ²	0	0	1	2	0	0	0	0	36	19	23	20
West Virginia.....	2.7	1	3	3	0	0	1	1	70	26	16	47
North Carolina.....	0	0	1	3	1.5	1	2	2	19	13	13	14
South Carolina.....	8	3	2	1	60	22	0	0	14	5	5	4
Georgia ²	0	0	0	0	1.7	1	0	0	10	6	2	2
Florida ²	0	0	2	1	3	1	3	0	27	9	1	1
E. SO. CEN.												
Kentucky.....	0	0	3	5	0	0	1	0	33	19	13	24
Tennessee ²	1.8	1	3	3	0	0	2	0	67	38	31	18
Alabama ²	5	3	5	3	1.8	1	1	0	18	10	6	5
Mississippi ²	0	0	1	0	0	0	0	0	3	1	2	2
W. SO. CEN.												
Arkansas.....	2.5	1	0	0	0	0	1	0	10	4	1	3
Louisiana.....	0	0	0	1	0	0	2	2	5	2	2	7
Oklahoma.....	0	0	0	0	0	0	0	0	20	10	21	19
Texas ²	0.8	1	0	3	1.7	2	0	0	25	30	70	50
MOUNTAIN												
Montana.....	9	1	1	1	0	0	0	0	131	14	12	12
Idaho ²	0	0	0	0	0	0	0	0	20	2	6	6
Wyoming ²	0	0	0	0	0	0	0	0	87	4	7	10
Colorado ²	0	0	1	0	0	0	1	0	159	33	37	37
New Mexico.....	0	0	0	0	0	0	0	0	49	4	9	9
Arizona.....	0	0	0	0	86	7	0	0	49	4	5	13
Utah ²	0	0	0	0	0	0	0	0	228	23	14	14
PACIFIC												
Washington.....	0	0	1	0	0	0	0	0	80	29	15	32
Oregon ²	0	0	1	1	5	1	0	0	55	11	19	25
California ²	1.6	2	2	2	14	17	2	5	112	137	155	175
Total.....	1.9	49	51	96	2.4	60	19	36	102	2,559	3,315	4,470
22 weeks.....	1.9	1,052	1,690	3,134	0.9	511	427	468	188	103,808	120,897	145,153

See footnotes at end of table.

Cases of certain diseases reported by telegraph by State health officers for the week ended June 3, 1939, rates per 100,000 population (annual basis), and comparison with corresponding week of 1938 and 5-year median—Continued

Division and State	Smallpox				Typhoid and paratyphoid fever				Whooping cough		
	June 3, 1939, rate	June 3, 1939, cases	June 4, 1938, cases	1934-38, median	June 3, 1939, rate	June 3, 1939, cases	June 4, 1938, cases	1934-38, median	June 3, 1939, rate	June 3, 1939, cases	June 4, 1938, cases
NEW ENG.											
Maine.....	0	0	0	0	0	0	1	2	163	27	22
New Hampshire.....	0	0	0	0	0	0	0	0	0	0	0
Vermont.....	0	0	0	0	0	0	2	0	523	39	20
Massachusetts.....	0	0	0	0	0	0	1	3	128	109	143
Rhode Island.....	0	0	0	0	0	0	0	1	328	43	24
Connecticut.....	0	0	0	0	3	1	0	2	134	45	76
MID. ATL.											
New York ¹	8	20	0	0	2	6	1	7	134	334	433
New Jersey ²	0	0	0	0	4	3	1	2	350	294	191
Pennsylvania ³	0	0	0	0	4	7	9	7	98	194	184
E. NO. CEN.											
Ohio ¹	22	28	69	0	12	16	8	7	130	169	133
Indiana.....	33	22	39	2	1	1	3	3	105	71	30
Illinois.....	7	10	15	15	5	7	5	6	153	233	230
Michigan ⁴	7	7	1	1	1	1	6	5	172	163	257
Wisconsin.....	2	1	2	2	2	1	3	1	246	140	191
W. NO. CEN.											
Minnesota.....	33	17	16	16	2	1	1	1	83	43	45
Iowa ²	61	30	21	21	4	2	1	0	51	25	34
Missouri.....	36	28	48	7	1	1	8	8	28	22	38
North Dakota.....	0	0	19	11	29	4	2	2	7	1	25
South Dakota.....	105	14	22	5	0	0	0	0	8	1	3
Nebraska.....	34	9	1	5	0	0	0	0	27	7	14
Kansas.....	17	6	23	13	0	0	1	2	78	28	134
SO. ATL.											
Delaware.....	0	0	0	0	0	0	1	0	394	30	9
Maryland ^{2,4}	0	0	0	0	6	2	5	5	108	35	47
Dist. of Col. ²	0	0	0	0	8	1	1	1	218	27	12
Virginia ²	0	0	0	0	11	6	6	7	240	128	147
West Virginia.....	0	0	1	0	16	6	5	5	89	33	14
North Carolina.....	0	0	6	1	13	9	8	5	288	197	240
South Carolina.....	0	0	0	0	25	9	8	8	188	69	69
Georgia ²	20	12	0	0	28	17	21	7	80	48	44
Florida ²	0	0	0	0	6	2	9	2	142	47	20
E. SO. CEN.											
Kentucky.....	2	1	2	0	9	5	4	6	26	15	43
Tennessee ³	97	55	1	1	16	9	9	8	123	70	66
Alabama ³	0	0	0	0	18	10	13	5	190	108	26
Mississippi ^{2,4}	0	0	1	0	8	3	6	4	—	—	—
W. SO. CEN.											
Arkansas.....	12	5	13	2	27	11	16	6	50	20	41
Louisiana.....	0	0	1	0	24	10	11	10	15	6	10
Oklahoma.....	89	40	32	4	14	7	11	6	6	—	60
Texas ²	6	7	34	24	10	12	34	24	107	129	373
MOUNTAIN											
Montana.....	19	2	5	5	0	0	1	1	56	6	43
Idaho ²	0	0	5	1	0	0	1	0	71	7	5
Wyoming ²	0	0	0	3	0	0	0	0	0	0	10
Colorado ^{2,3}	29	6	4	3	5	1	7	0	135	28	21
New Mexico.....	12	1	0	0	0	0	0	2	222	18	12
Arizona.....	37	3	9	0	12	1	3	3	61	5	24
Utah ^{2,4}	10	1	0	0	30	3	0	0	467	47	80
PACIFIC											
Washington.....	9	3	22	3	86	28	1	1	49	16	113
Oregon ²	35	7	28	2	0	0	3	3	85	17	38
California ²	2	2	18	8	6	7	7	7	148	181	421
Total.....	13	337	458	198	8	210	244	197	132	3,268	4,305
22 weeks.....	14	7,649	10,894	4,855	5	2,720	2,966	2,966	160	87,076	94,258

¹ New York City only.

² Rocky Mountain spotted fever, week ended June 3, 1939, 26 cases as follows: New York, 1; New Jersey, 2; Ohio, 3; Iowa, 2; Maryland, 1; District of Columbia, 2; Virginia, 4; Idaho, 1; Wyoming, 3; Colorado, 3; Utah, 2; Oregon, 2.

³ Typhus fever, week ended June 3, 1939, 48 cases as follows: Pennsylvania, 1; Georgia, 17; Florida, 4; Tennessee, 5; Alabama, 9; Mississippi, 3; Texas, 8; California, 1.

⁴ Period ended earlier than Saturday.

⁵ Colorado tick fever, week ended June 3, 1939, Colorado, 15 cases.

SUMMARY OF MONTHLY REPORTS FROM STATES

The following summary of cases reported monthly by States is published weekly and covers only those States from which reports are received during the current week.

State	Menin- gitis, menin- gococ- cus	Diph- theria	Infl- enza	Ma- laria	Mea- sles	Pel- lagra	Polio- mye- litis	Scarlet fever	Small- pox	Ty- phoid and paraty- phoid fever
<i>March 1939</i>										
Puerto Rico.....	0	40	154	2,362	9	3	0	0	0	41
<i>April 1939</i>										
Wisconsin.....	2	1	449	-----	2,901	-----	1	734	5	1
<i>May 1939</i>										
Missouri.....	2	16	4	4	41	-----	0	268	148	4

<i>March 1939</i>		<i>April 1939</i>		<i>May 1939</i>	
Puerto Rico:	Cases	Wisconsin:	Cases	Missouri:	Cases
Chickenpox.....	66	Chickenpox.....	1,196	Chickenpox.....	171
Dysentery.....	7	Encephalitis, epidemic or lethargic.....	1	Dysentery (bacillary)...	3
Leprosy.....	2	German measles.....	89	Mumps.....	327
Mumps.....	5	Mumps.....	1,075	Rabies in man.....	3
Ophthalmia neonatorum.....	4	Septic sore throat.....	27	Septic sore throat.....	18
Puerperal septicemia.....	7	Undulant fever.....	10	Tetanus.....	1
Tetanus.....	8	Whooping cough.....	655	Trachoma.....	48
Tetanus, infantile.....	2			Tularaemia.....	3
Whooping cough.....	180			Whooping cough.....	78

PLAGUE INFECTION IN CALIFORNIA AND OREGON

IN A GROUND SQUIRREL IN VENTURA COUNTY, CALIF.

Under date of May 26, 1939, Dr. W. M. Dickie, State Director of Public Health of California, reported plague infection proved in a ground squirrel, *C. beecheyi*, submitted to the laboratory on April 26 from a location 5 miles north of Ventura, in Mills Canyon, Ventura County, Calif.

IN FLEAS FROM GROUND SQUIRRELS IN GRANT COUNTY, OREG.

Under date of May 29, 1939, Senior Surg. C. R. Eskey reported plague infection proved in a pool of 13 fleas from 28 ground squirrels, *C. oregonus*, shot May 10 at localities 1 to 4 miles south of Mount Vernon, Grant County, Oreg.

WEEKLY REPORTS FROM CITIES

City reports for week ended May 27, 1939

This table summarizes the reports received weekly from a selected list of 149 cities for the purpose of showing a cross section of the current urban incidence of the communicable diseases listed in the table.

State and city	Diphtheria cases	Influenza		Measles cases	Pneumonia deaths	Scarlet fever cases	Smallpox cases	Tuberculosis deaths	Typhoid fever cases	Whooping cough cases	Deaths, all causes
		Cases	Deaths								
Data for 90 cities:											
5-year average	154	72	32	6,059	562	1,963	17	406	32	1,341	-----
Current week ¹	100	90	33	4,171	400	1,232	25	341	32	1,130	-----
Maine:											
Portland	0		0	0	2	1	0	0	0	9	18
New Hampshire:											
Concord	0		0	0	0	0	0	1	0	0	10
Manchester	0		0	0	0	0	0	0	0	0	9
Nashua	0		0	0	0	0	0	0	0	0	6
Vermont:											
Barre	0			0		1	0		0	14	-----
Burlington	0		0	9	0	0	0	0	0	4	7
Rutland	0		0	0	2	0	0	0	0	0	8
Massachusetts:											
Boston	2		0	201	27	56	0	8	0	26	203
Fall River	1		0	3	1	4	0	0	0	0	32
Springfield	0		0	14	1	1	0	0	0	2	27
Worcester	0		0	22	5	2	0	2	0	16	52
Rhode Island:											
Pawtucket	0		0	33	3	1	0	0	0	2	3
Providence	0	35	0	66	5	6	0	3	1	34	61
Connecticut:											
Bridgeport	0		1	15	3	2	0	1	0	1	30
Hartford	0		0	22	2	4	0	3	0	7	40
New Haven	0		1	297	1	6	0	1	1	10	36
New York:											
Buffalo	0		1	135	10	45	0	4	0	11	163
New York	19	8	2	218	48	217	0	60	6	117	1,396
Rochester	0	2	0	183	2	19	0	2	1	6	69
Syracuse	0		0	255	2	4	0	0	0	21	33
New Jersey:											
Camden	1		0	0	0	5	0	0	0	1	26
Newark	0	2	0	2	4	61	0	9	0	57	100
Trenton	0		0	0	4	15	0	0	0	2	46
Pennsylvania:											
Philadelphia	5	2	2	61	25	26	0	26	1	63	479
Pittsburgh	3		1	1	15	24	0	10	2	32	154
Reading	0		0	15	0	0	0	1	0	0	24
Scranton	0			0		8	0		0	1	-----
Ohio:											
Cincinnati	3		5	2	8	25	0	3	0	1	115
Cleveland	4	10	0	8	12	64	0	13	0	54	188
Columbus	0		0	4	2	3	0	2	0	13	101
Toledo	0		0	24	3	17	2	2	0	39	65
Indiana:											
Anderson	0		0	0	1	2	0	0	0	4	13
Fort Wayne	0		0	0	0	4	0	0	0	0	17
Indianapolis	1		0	1	7	33	6	3	1	44	89
Muncie	0		0	1	0	0	0	0	0	0	10
South Bend	0		0	1	1	1	0	0	0	34	19
Terre Haute	0		0	0	4	0	0	0	0	0	37
Illinois:											
Alton	0		0	0	1	2	0	0	0	0	10
Chicago	16	2	2	14	19	194	2	40	1	107	665
Elgin	0		1	1	0	1	0	0	0	5	10
Moline	0		0	0		0	0		0	3	-----
Springfield	0		0	0	1	1	0	0	0	5	19
Michigan:											
Detroit	6		0	29	11	103	0	9	1	89	249
Flint	0		1	28	4	22	0	0	0	1	34
Grand Rapids	0		0	2	0	37	0	1	0	0	30
Wisconsin:											
Kenosha	0		0	0	0	3	0	0	0	4	11
Madison	0		0	153	0	1	0	0	0	11	13
Milwaukee	0		0	3	3	33	0	7	0	31	101
Racine	0		0	2	1	1	0	0	0	5	11
Superior	0		0	10	0	2	0	0	0	1	6

¹ Figures for Little Rock and Houston estimated; reports not received.

City reports for week ended May 27, 1939—Continued

State and city	Diph- theria cases	Influenza		Mea- sles cases	Pneu- monia deaths	Scar- let fever cases	Small- pox cases	Tuber- culosis deaths	Ty- phoid fever cases	Whoop- ing cough cases	Deaths, all causes
		Cases	Deaths								
Minnesota:											
Duluth.....	0		0	0	2	0	0	3	0	2	27
Minneapolis.....	0		1	79	3	10	0	2	0	26	93
St. Paul.....	0	1	1	50	5	6	0	0	0	13	62
Iowa:											
Cedar Rapids.....	0			7		1	0		0	0	
Davenport.....	0			0		1	5		0	0	
Des Moines.....	0		0	1	0	20	4	0	0	0	40
Sioux City.....	0			7		4	0		0	12	
Waterloo.....	2			1		9	0		0	1	
Missouri:											
Kansas City.....	2		1	4	8	13	0	4	0	2	95
St. Joseph.....	0		0	0	0	0	0	1	0	0	27
St. Louis.....	2		1	2	8	20	0	8	1	19	191
North Dakota:											
Fargo.....	0		0	3	1	0	0	0	0	0	9
Grand Forks.....	0			0		0	0		0	0	
Minot.....	0		0	0	0	0	0	0	0	1	2
South Dakota:											
Aberdeen.....	0			235		0	12		0	0	
Sioux Falls.....	0		0	1	0	3	6	0	0	0	4
Nebraska:											
Lincoln.....	0			66		2	0		0	15	
Omaha.....	1		0	3	3	3	3	0	1	2	49
Kansas:											
Lawrence.....	0		0	1	0	1	0	0	0	0	5
Topeka.....	0		0	1	3	2	6	1	0	2	18
Wichita.....	0		0	8	3	1	0	0	1	9	22
Delaware:											
Wilmington.....	0		0	12	2	1	0	1	0	0	25
Maryland:											
Baltimore.....	2	2	1	67	6	19	0	14	1	26	201
Cumberland.....	0		0	0	0	0	0	0	0	0	6
Frederick.....	0		0	0	0	0	0	0	0	0	2
Dist. of Col.:											
Washington.....	3		0	316	10	13	0	13	1	27	169
Virginia:											
Lynchburg.....	1		0	71	1	0	0	1	0	22	14
Norfolk.....	3	1	0	39	1	2	0	1	0	3	33
Richmond.....	1		2	342	3	1	0	0	0	0	45
Roanoke.....	0		0	1	0	0	0	0	0	2	16
West Virginia:											
Charleston.....	0		0	0	1	0	0	0	1	0	11
Huntington.....	2			0		1	0		0	0	
Wheeling.....	0		0	1	1	1	0	0	0	10	22
North Carolina:											
Gastonia.....	0			0		0	0		0	0	
Raleigh.....	1		0	3	1	0	0	0	0	0	12
Wilmington.....	0		0	1	2	0	0	0	0	0	9
Winston-Salem.....	0		0	5	1	1	0	4	0	1	27
South Carolina:											
Charleston.....	0	2	0	0	1	0	0	1	0	6	20
Greenville.....	0		0	0	1	0	0	0	0	0	4
Georgia:											
Atlanta.....	1	7	2	1	2	1	0	4	1	1	79
Brunswick.....	0		0	6	0	1	0	0	0	0	3
Savannah.....	0	2	0	0	2	0	0	2	0	8	24
Florida:											
Miami.....	1	2	0	1	1	1	0	2	1	3	31
Tampa.....	0	1	1	31	4	1	0	0	0	4	22
Kentucky:											
Ashland.....	0		0	0	0	0	0	0	0	0	5
Covington.....	0		0	0	1	2	0	3	0	0	13
Lexington.....	0		0	0	1	0	0	0	0	1	17
Louisville.....	0	1	0	4	5	9	0	1	0	6	38
Tennessee:											
Knoxville.....	0	1	1	0	0	2	0	0	1	0	17
Memphis.....	0		3	2	3	12	0	5	1	15	76
Nashville.....	0		1	0	2	7	0	1	0	1	65
Alabama:											
Birmingham.....	0	1	0	1	2	1	0	1	0	6	66
Mobile.....	0	3	0	24	3	0	0	0	0	1	24
Montgomery.....	0			1		1	0		0	2	

City reports for week ended May 27, 1939—Continued

State and city	Diph- theria cases	Influenza		Meas- les cases	Pneu- monia deaths	Scar- let fever cases	Small- pox cases	Tuber- culosis deaths	Ty- phoid fever cases	Whoop- ing cough cases	Deaths, all causes
		Cases	Deaths								
Arkansas:											
Fort Smith.....	1			5		1	0		0	0	
Little Rock.....											
Louisiana:											
Lake Charles.....	0		0	0	1	0	0	0	0	0	7
New Orleans.....	2	1	1	27	7	7	0	11	2	1	130
Shreveport.....	1		0	6	0	1	0	2	0	1	40
Oklahoma:											
Oklahoma City.....	0	2	0	3	4	3	1	0	0	0	47
Tulsa.....	0			30		2	0		0	0	
Texas:											
Dallas.....	3		0	30	4	1	0	2	0	0	72
Fort Worth.....	0	1	0	15	0	1	0	3	0	3	31
Galveston.....	0		0	0	1	0	0	0	0	1	15
Houston.....											
San Antonio.....	0		2	0	3	0	0	4	0	0	69
Montana:											
Billings.....	0		0	0	2	0	0	0	0	0	11
Great Falls.....	0		0	120	1	0	0	0	0	0	9
Helena.....	0			0		0	0		0	0	
Missoula.....	0		0	0	1	0	0	0	0	0	12
Idaho:											
Boise.....	0		0	8	1	0	0	0	0	1	
Colorado:											
Colorado Springs.....	0		0	4	2	5	0	1	0	1	17
Denver.....	5		0	57	2	22	0	5	0	23	87
Pueblo.....	0		0	90	0	0	0	0	0	13	9
New Mexico:											
Albuquerque.....	0		0	0	1	1	0	2	0	0	11
Utah:											
Salt Lake City.....	0		0	3	0	8	0	2	0	13	33
Washington:											
Seattle.....	1		0	517	5	4	0	3	2	2	63
Spokane.....	0		0	126	2	1	0	0	0	0	39
Tacoma.....	1		0	16	2	0	2	0	0	0	35
Oregon:											
Portland.....	0		0	3	0	3	0	1	0	4	69
Salem.....	0			0		0	0		0	0	
California:											
Los Angeles.....	11	9	0	403	21	37	0	18	1	29	318
Sacramento.....	0		0	67	1	1	6	1	0	1	36
San Francisco.....	0		0	22	8	10	0	12	4	10	160

State and city	Meningitis, meningococcus		Polio- mye- litis cases	State and city	Meningitis, meningococcus		Polio- mye- litis cases
	Cases	Deaths			Cases	Deaths	
Massachusetts:				Wisconsin:			
Springfield.....	1	0	0	Kenosha.....	0	0	1
Worcester.....	1	0	0	Milwaukee.....	1	0	0
New York:				South Carolina:			
Buffalo.....	0	1	0	Charleston.....	0	0	9
New York.....	1	0	1	Georgia:			
Pennsylvania:				Atlanta.....	0	0	1
Philadelphia.....	2	0	0	Kentucky:			
Illinois:				Lexington.....	1	0	0
Moline.....	0	0	1	Colorado:			
				Denver.....	1	1	0

Encephalitis, epidemic or lethargic.—Cases: New York, 1; St. Paul, 1; Cumberland, 1.

Pellagra.—Cases: Winston-Salem, 3; Atlanta, 1; Savannah, 3; Miami, 1; New Orleans, 1; San Francisco, 1.

Typhus fever.—Cases: New York, 1; Brunswick, 1; Montgomery, 1; New Orleans, 1.

FOREIGN AND INSULAR

CANADA

Provinces—Communicable diseases—Week ended May 13, 1939.—During the week ended May 13, 1939, cases of certain communicable diseases were reported by the Department of Pensions and National Health of Canada as follows:

Disease	Prince Edward Island	Nova Scotia	New Brunswick	Quebec	Ontario	Manitoba	Saskatchewan	Alberta	British Columbia	Total
Cerebrospinal meningitis				1	2	1				4
Chickenpox		16		153	146	13	12	1	49	390
Diphtheria		7	2	31	4	9	3			56
Dysentery				4	2					6
Influenza		30			307		3		178	518
Lethargic encephalitis					3					3
Measles		24		231	726	8		16	6	1,011
Mumps				37	99	50		1	4	191
Pneumonia		12			45			1	11	69
Polio-myelitis		1						2		3
Scarlet fever		4	17	68	120	31	10	18	6	274
Tuberculosis	2	1	16	126	54	6	4	3		212
Typhoid and paratyphoid fever			1	20	2	14		1		38
Whooping cough		14	2	72	170	7	41	31	72	409

CUBA

Provinces—Notifiable diseases—4 weeks ended April 1, 1939.—During the 4 weeks ended April 1, 1939, cases of certain notifiable diseases were reported in the Provinces of Cuba as follows:

Disease	Pinar del Rio	Habana	Matanzas	Santa Clara	Camaguey	Oriente	Total
Cancer	2	1		6		3	12
Chickenpox		5	1		1	2	9
Diphtheria	3	23	3	2	1	2	34
Leprosy	1					2	3
Malaria	24	6	1	9	6	40	86
Measles				3		1	4
Scarlet fever		2					2
Trachoma						1	1
Tuberculosis	15	19	36	64	10	61	205
Typhoid fever	8	70	12	33	14	14	151

SWITZERLAND

Communicable diseases—March 1939.—During the month of March 1939, cases of certain communicable diseases were reported in Switzerland as follows:

Disease	Cases	Disease	Cases
Cerebrospinal meningitis	5	Mumps	170
Chickenpox	142	Paratyphoid fever	5
Diphtheria	69	Scarlet fever	382
German measles	15	Tuberculosis	315
Influenza	4,641	Typhoid fever	5
Lethargic encephalitis	2	Undulant fever	12
Measles	18	Whooping cough	78

CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER

NOTE.—A table giving current information of the world prevalence of quarantinable diseases appeared in the PUBLIC HEALTH REPORTS for May 26, 1939, pages 906-918. A similar cumulative table will appear in future issues of the PUBLIC HEALTH REPORTS for the last Friday of each month.

Cholera

China—Macao.—During the week ended May 27, 1939, 10 cases of cholera were reported in Macao, China.

India—Allahabad.—During the week ended May 27, 1939, 1 case of cholera was reported in Allahabad, India.

Plague

Belgian Congo—Virakwa—Drodro.—During the week ended May 27, 1939, 11 cases of plague were reported in Drodro, Virakwa, Belgian Congo.

China—Manchuria—Hsinking.—According to information dated May 5, 1939, 34 cases of plague have occurred in Hsinking, Manchuria, since the beginning of the year, as compared with 17 cases in the first 4 months of 1938. Only 8 deaths have been reported and all preventive measures have been taken.

Hawaii Territory—Island of Hawaii—Hamakua District—Kapulena.—Two rats found on May 6, 1939, in the Kapulena area, Hamakua District, Island of Hawaii, Hawaii Territory, have been proved positive for plague.

United States.—A report of plague infection in Ventura County, Calif., and in Grant County, Oreg., appears on page 1084 of this issue of the PUBLIC HEALTH REPORTS.

Typhus Fever

Venezuela—Bolivar State—Bolivar.—During the period April 16-30, 1939, 1 case of typhus fever was reported in Bolivar, Bolivar State, Venezuela.

Yellow Fever

Ivory Coast.—On May 25, 1939, yellow fever was reported in Ivory Coast as follows: Arra region, 1 case; Tranin Plantation near Man, 1 case.

French West Africa—Niger—Tahua.—On May 24, 1939, 1 case of yellow fever was reported in Tahua, Niger, French West Africa.